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(54) Sulfonamide derivatives

Sulfonamid-Derivate

Dérivés de sulfonamide

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(73) Proprietor: **Eisai Co., Ltd.**
Tokyo (JP)

(72) Inventors:
- **Yoshino, Hiroshi**
  Abiko-shi, Chiba (JP)
- **Ueda, Norihiro**
  Tsukuba-shi, Ibaraki (JP)
- **Sgumi, Hiroyuki**
  Tsukuba-shi, Ibaraki (JP)
- **Niijima, Jun**
  Tsukuba-shi, Ibaraki (JP)
- **Kotake, Yoshihiko**
  Tsukuba-shi, Ibaraki (JP)
- **Okada, Toshimi**
  Tsukuba-shi, Ibaraki (JP)
- **Koyanagi, Nozomu**
  Tsukuba-shi, Ibaraki (JP)
- **Watanabe, Tatsuo**
  Kita-ku, Osaka-shi, Osaka (JP)
- **Asada, Makoto**
  Tsukuba-shi, Ibaraki (JP)
- **Yoshimatsu, Kentaro**
  Tsuchiura-shi, Ibaraki (JP)
- **Iijima, Atsumi**
  Niihari-gun, Ibaraki (JP)
- **Nagasu, Takeshi**
  Tsuchiura-shi, Ibaraki (JP)
- **Tsukahara, Kappei**
  Tsukuba-shi, Ibaraki (JP)
- **Kitoh, Kyosuke**
  Tsukuba-shi, Ibaraki (JP)

(74) Representative:
Hansen, Bernd, Dr. Dipl.-Chem. et al
Hoffmann Eitle,
Patent- und Rechtsanwälte,
Postfach 81 04 20
81904 München (DE)

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Description

The present invention relates to new sulfonamide derivatives, processes for producing them and a medicinal composition containing the same as the active ingredient.

Chemotherapeutic agents for cancers used heretofore include various substances, for example, alkylating agents such as cyclophosphamide, antimetabolites such as methotrexate and fluorouracil, antibiotics such as adriamycin, mitomycin and bleomycin, those derived from plants such as vincristine and etoposide, and metal complexes such as cisplatin.

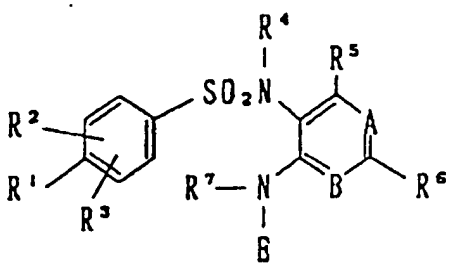
4-Aminobenzenesulfonamide derivatives (see Japanese Patent Publication No. 3093/1968), 2-sulfanylamide/quinoxaline derivatives (see EP-A-215200 and Japanese Patent Laid-Open No. 426/1987) and m-AMSA derivatives (see J. Med. Chem., 18, 1110 (1975)) were reported as active antineoplastic compounds having a sulfonamide group.

Most of them have only a low effectiveness on human tumors, particularly solid tumors having a low growth rate, such as lung cancer or colon cancer, and exhibit serious adverse reactions. Under these circumstances, a development of a new medicine having only a low toxicity and an excellent antitumor activity is demanded.

An object of the present invention is to provide new sulfonamide derivatives having an excellent antitumor activity and only a low toxicity. Another object of the present invention is to provide a process for producing these compounds and a medicinal composition containing them as the active ingredient.

After intensive investigations made for the purpose of finding an antitumor compound having only a low toxicity as described above, the inventors have found that new sulfonamide derivatives which will be described below have an excellent antitumor activity and only a low toxicity. The present invention has been completed on the basis of this finding.

Thus the present invention relates to sulfonamide derivatives of the general formula (I) or pharmacologically acceptable salts of them:

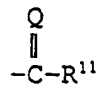


(I)

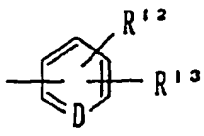
wherein:

R^1 represents a hydrogen atom, halogen atom, C_{1-6} alkyl group, C_{1-6} alkoxy group, hydroxyl group, nitro group, phenoxy group, cyano group, acetyl group or amino group which may be protected,
R^2 and R^3 may be the same or different from each other and each represent a hydrogen atom, halogen atom, C_{1-6} alkyl group or C_{1-6} alkoxy group,
R^4 and R^7 may be the same or different from each other and each represent a hydrogen atom or C_{1-6} alkyl group,
R^5 and R^6 may be the same or different from each other and each represent a hydrogen atom, halogen atom, C_{1-6} alkoxyl group or amino group which may be substituted,
A represents a group of the formula: =N- or =CH-,
B represents a group of the formula: =N- or

in which R^{10} represents a hydrogen atom or C_{1-6} alkyl group,
E represents a group of the formula:



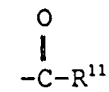
in which Q represents an oxygen atom or sulfur atom and R^{11} represents a hydrogen atom, C_{1-6} alkyl group, amino group which may be substituted with a lower alkyl group, C_{1-6} alkoxy group, 2-thienyl group, 2-furyl group or group of the formula:



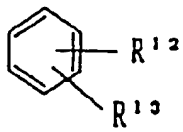
(D being a group of the formula: =N- or =CH-, and R^{12} and R^{13} being the same or different from each other and each being a hydrogen atom, halogen atom, nitro group, hydroxyl group which may be protected or C_{1-6} alkyl group); or an aromatic 6-memberred cyclic group which may be subtituted with 1 to 3 substituents G which may be the same or different from one another and which cyclic group may have 1 or 2 nitrogen atoms in the ring (G being a halogen atom, C_{1-6} alkyl group, C_{1-6} alkoxy group, hydroxyl group which may be protected, carboxyl group which may be esterified or amidated, C_{1-6} alkylthio group or phenoxy group,

with the proviso that the following combinations are excluded:

(1) a combination of R^1 which is a hydrogen atom, C_{1-6} alkyl group, nitro group or amino group which may be protected, R^2 and R^3 which are each hydrogen atom, A and B which are each =CH- and E which is a phenyl group which may be substituted with 1 to 3 substituents G which may be the same or different from one another, and
(2) a combination of R^1, R^2 and R^3 which may be the same or different from one another and which are each a hydrogen atom, lower alkyl group, nitro group, halogen atom, or acetylamino group A and B which are each =CH-, and E which is a group of the formula:



in which R^{11} is a C_{1-6} alkyl group, amino group which may be substituted with a C_{1-6} alkyl group or a group of the formula:



(R^{12} and R^{13} being each as defined above).

The detailed description will now be made on the present invention.

The C_{1-6} alkyl groups in the definition of R^1, R^2, R^3, R^4, R^7, R^{10}, R^{11}, R^{12}, R^{13} and the substituent G which may be substituted in the definition of E of the above general formula (I) include straight-chain and branched alkyl groups having 1 to 6 carbon atoms, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl (amyl), isopentyl, neopentyl, tert-pentyl, 1-methylbutyl, 2-methylbutyl, 1,2-dimethylpropyl, n-hexyl, isohexyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 1,1-dimethylbuty, 1,2-dimethylbutyl, 2,2-dimethylbutyl, 1,3-dimethylbutyl,

2,3-dimethylbutyl, 3,3-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-trimethylpropyl, 1-ethyl-1-methylpropyl and 1-ethyl-2-methylpropyl groups. Among them, preferred are methyl, ethyl, propyl and isopropyl groups and still preferred are methyl and ethyl groups.

The C_{1-6} alkoxy groups in the definition of R^1, R^2, R^3, R^5, R^6, R^{11} and the substituent G which may be substituted in the definition of E are those derived from the above-described C_{1-6} alkyl groups, such as methoxy, ethoxyl, n-propoxy, isopropoxy, n-butoxy, isobutoxy and t-butoxy groups. Among them, the most desirable are methoxy and ethoxy groups. The halogen atoms include fluorine, chlorine and bromine atoms.

The substituted amino groups in the definition of R^5 and R^6 include amino groups substituted with a C_{1-6} alkyl group (such as methylamino, ethylamino and dimethylamino groups) and amino groups substituted with a phenyl group.

The hydroxyl groups which may be protected of the substituent G which may be substituted in the definition of E include hydroxyl, methoxymethyloxy, tetrahydropyranyloxy, benzyloxy, phosphoric ester, sulfuric ester, sulfonic ester (such as ester with p-methoxybenzenesulfonic acid or methanesulfonic acid), amino acid ester (such as ester with glycine, alanine, leucine, tyrosine, aspartic acid, glutamic acid, lysine, arginine, proline, sarcosine, β-alanine or γ-aminobutyric acid), glycoside (such as glucoside and glucuronide), carbamoyloxy which may be substituted with a C_{1-6} alkyl (such as carbamoyloxy, methylcarbamoyloxy and dimethylcarbamoyloxy), C_{1-6} acyloxy (having 1 to 5 carbon atoms such as formyloxy, acetoxy, propionyloxy and pivaloyloxy) and benzoyloxy.

The aromatic ring of the benzoyloxy group may be, if desired, substituted with a C_{1-6} alkyl group such as a methyl, ethyl, n-propyl or isopropyl group, a C_{1-6} alkoxy group such as a methoxy, ethoxy, n-propoxy or isopropoxy group, a halogen atom such as a fluorine, chlorine or bromine atom or an amino group which may be substituted with a C_{1-6} alkyl group.

The amino groups which may be protected in the definition of R^1 include unsubstituted amino group, lower acylamino groups (having 1 to 4 carbon atoms such as formylamino, acetamino and propionylamino groups) and benzyloxycarbonylamino group.

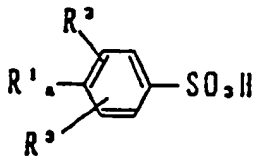
The carboxyl groups which may be esterified or amidated in the definition of the substituent G which may be substituted in the definition of E include carboxyl group, lower alkoxycarbonyl groups (having 2 to 5 carbon atoms such as methoxycarbonyl, ethoxycarbonyl and isopropyloxycarbonyl groups), unsubstituted aminocarbonyl group, and aminocarbonyl groups substituted with an alkyl group having 1 to 4 carbon atoms (such as methylaminocarbonyl, ethylaminocarbonyl and dimethylaminocarbonyl groups).

The sulfonamide derivatives represented by the above general formula (I) may form a salt with an acid or base. The salts of the compounds (I) are also included in the present invention. Examples of the salts of them with an acid include inorganic acid salts such as hydrochloride, hydrobromide and sulfate as well as organic acid salts such as acetate, lactate, succinate, fumarate, maleate, citrate, benzoate, methanesulfonate and p-toluenesulfonate. Examples of the salts of them with a base include inorganic salts such as sodium, potassium and calcium salts and salts with organic bases such as triethylamine, arginine and lysine.

As a matter of course, hydrates of these compounds and optical isomers, if present, are also included in the present invention. The compounds of the present invention exhibit a potent antineoplastic activity. Compounds which exhibit an antineoplastic activity upon undergoing metabolism such as oxidation, hydrolysis or conjugation in vivo are also included in the present invention.

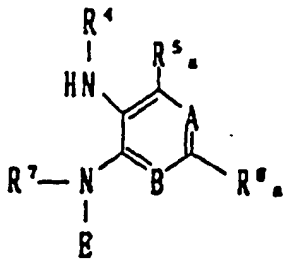
The compounds (I) of the present invention can be produced by various processes. Typical processes among them are as follows:

(1) A sulfonic acid of the general formula (II) or its reactive derivative:



(II)

wherein R^2 and R^3 are as defined above and $R^1{}_a$ represents a hydrogen atom, halogen atom, or lower alkyl, lower alkoxy protected hydroxyl, nitro, phenoxy, cyano, acetyl or protected amino group, is reacted with a compound of the general formula (III) :



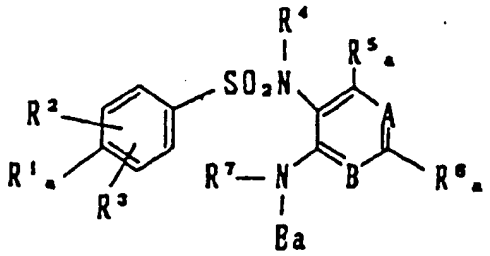
(III)

wherein R^4, R^7, A, B and E are each as defined above, and $R^5{}_a$ and $R^6{}_a$ may be the same or different from each other and each represent a hydrogen or halogen atom, lower alkoxy, or protected or substituted amino group.

The reactive derivatives of the sulfonic acids (II) include those usually often used, such as sulfonyl halide, sulfonil anhydride and N-sulfonylimidazolide. Among them, particularly preferred is sulfonyl halide. The reaction proceeds when they are used in stoichiometrically equimolar amounts. Although the solvents used for the reaction are not particularly limited, desirable solvents are those in which the starting materials are soluble and which do not easily react with the starting materials. The solvents are, for example, pyridine, tetrahydrofuran, dioxane, benzene, ether, methylene chloride, dimethylformamide and mixtures of two or more of them. When an acid is liberated as the reaction proceeds as in the case a sulfonyl halide, the reaction is desirably conducted in the presence of a suitable acid binder. Therefore, the use of a basic solvent such as pyridine is particularly preferred. When a neutral solvent is used, a basic substance such as an alkali carbonate or an organic tertiary amine may be added. As a matter of course, the solvents usable herein are not limited to those described above. The reaction usually proceeds at room temperature and, if desired, it may be conducted under cooling or heating. The reaction time usually ranges from 10 min to 20 h. It is suitably determined depending on the varieties of the starting compounds and reaction temperature.

When the amino, hydroxyl or carboxyl group in the resulting sulfonamide derivative (I) is protected, it can be subjected to an ordinary method of removing protective groups, such as an acid treatment, alkali treatment or catalytic reduction, if desired, to obtain a compound (I) having a free hydroxyl, amino or carboxyl group.

(2) A compound of the general formula (IV)



(IV)

wherein $R^1{}_a$, R^2, R^3, R^4, $R^5{}_a$, $R^6{}_a$, R^7, A and B are each as defined above, and Ea represents an aromatic 6-membered cyclic group (which may contain 1 or 2 nitrogen atoms in the ring) substituted with 1 to 3 substituents Ga which may be the same or different from one another, Ga being a halogen atom, lower alkyl group, lower alkoxy group, hydroxyl group, carboxyl group which may be esterified or amidated, lower alkylthio group or phenoxy group with the proviso that at least one Ga on the ring is a hydroxyl group,
is reacted with a compound of the general formula (V):

X-Y (V)

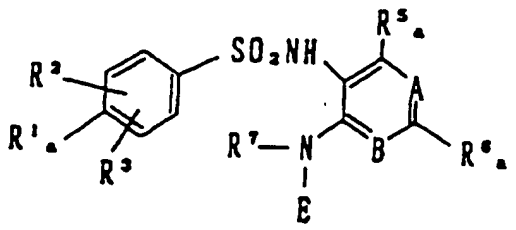
wherein X represents a group capable of bonding with the oxygen atom of the hydroxyl group and Y represents a removable group,
or with an inorganic acid or organic acid anhydride reactive with the hydroxyl group.

X-Y include reactive derivatives of aromatic and aliphatic sulfonic acids, aromatic and aliphatic carboxylic acids, amino acids which may be protected, phosphoric acid which may be protected, sulfuric acid which may be

protected, carbamic acid which may be substituted with a lower alkyl group and saccharides which may be protected. Examples of them include p-methoxybenzenesulfonyl chloride, methanesulfonyl chloride, o-chlorobenzoyl chloride, acetyl chloride, N-(t-butoxycarbonylaminoacetyl)imidazole, phosphorus oxychloride, chlorosulfonic acid, N,N-dimethylcarbamoyl chloride and methyl 1,2,3,4-tetra-O-acetyl-D-glucuronate. Examples of the anhydrides include inorganic acid anhydrides such as diphosphorus pentaoxide and sulfur trioxide as well as organic acid anhydrides such as N-carboxy anhydrides (NCA) of α-amino acids and isatoic anhydride.

Although the solvents used in the reaction are not particularly limited, desirable solvents are those in which the starting materials are soluble and which do not easily react with the starting materials. The solvents are, for example, pyridine, tetrahydrofuran, dioxane, benzene, ether, methylene chloride, dimethylformamide and mixtures of two or more of them. When a liquid starting compound such as phosphorus oxychloride is used, the reaction can be conducted without using any solvent.

(3) A compound of the general formula (VI):



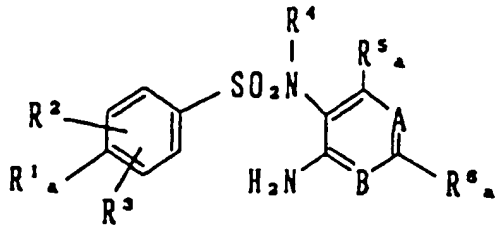
(VI)

wherein R^1_a, R^2, R^3, R^5_a, R^6_a, R^7, A, B and E are each as defined above, is reacted with a compound of the general formula:

$$R^4_a\text{-}L$$

wherein R^4_a represents a lower alkyl group and L represents a halogen atom, in the presence of a base such as sodium hydride.

(4) A compound of the general formula (VII):



(VII)

wherein R^1_a, R^2, R^3, R^4, R^5_a, R^6_a, A and B are each as defined above, is reacted with a compound of the general formula (VIII):

$$R^{11}\text{-}Z \qquad \text{(VIII)}$$

wherein R^{11} is as defined above, and Z represents a carboxyl group or its reactive derivative, or when R^{11} is a lower alkylamino group, it is reacted with a lower alkyl isocyanate.

The reactive derivatives of the carboxylic acids usable herein are, for example, acid halides, acid anhydrides, active amide compounds and active esters.

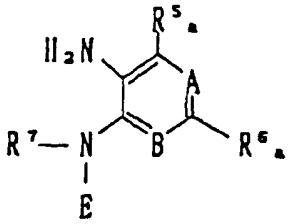
Examples of the acid halides usable herein are, for example, acid chlorides and acid bromides. The acid anhydrides usable herein are, for example, mixed monoalkylcarbonic acid anhydrides, mixed acid anhydrides comprising aliphatic carboxylic acids (such as acetic acid, pivalic acid, valeric acid, isovaleric acid and trichloroacetic acid), mixed aromatic carboxylic acids (such as benzoic acid) and symmetric acid anhydrides. The active amide compounds usable herein are, for example, amides of acids with imidazole, pyrazole, 4-substituted imidazole, dimethylpyrazole, triazole, tetrazole and benzothiazole. The active esters are suitably selected from among methyl esters, methoxymethyl esters, cyanomethyl esters, propargyl esters, 4-nitrophenyl esters, 2,4-dinitrophenyl esters, trichlorophenyl esters, pentachlorophenyl esters, methanesulfonylphenyl esters, phenylazophenyl esters and esters with 1-hydroxy-1H-2-pyridone, N-hydroxysuccinimide, N-hydroxyphthalimide or 1-hydroxybenzotriazole.

The carboxylic acid (VIII) can be reacted with the amine (VII) in the presence of a condensing agent such as N, N'-dicyclohexylcarbodiimide (DCC) or N-cyclohexyl-N'-morpholinoethylcarbodiimide.

When R^{11} is an amino group substituted with a lower alkyl group, the amine (VII) may be reacted with a lower alkyl isocyanate. When R^{11} is an amino group, the amine (VII) may be reacted with an alkali metal salt of cyanic acid.

These reactions can be conducted in the presence of a base such as an organic tertiary amine (e.g. triethylamine, N,N-dimethylaniline or pyridine), alkali carbonate or alkali hydrogencarbonate or an acid, if necessary. The reaction proceeds when the reactants are used each in a stoichiometrically equimolar amount. Although the solvents used in the reaction are not particularly limited, desirable solvents are those in which the starting materials are soluble and which do not easily react with the starting materials. The solvents are, for example, pyridine, tetrahydrofuran, dioxane, benzene, ether, methylene chloride, dimethylformamide and mixtures of two or more of them. When a reagent difficultly soluble in the organic solvent, such as a cyanate, is used, the reaction may be conducted under hydrous conditions. The solvents usable herein are not limited to those described above. The reaction temperature is not particularly limited so far as the reaction proceeds. It is usually room temperature and, if desired, the reaction may be conducted under cooling or heating. The reaction time usually ranges from 5 min to 20 h. It is suitably determined depending on the varieties of the starting compounds and reaction temperature. When the product has a protected hydroxyl or amino group, it can be subjected to an ordinary method of removing protective groups, such as an acid treatment, alkali treatment or catalytic reduction to obtain a compound (I) having a free hydroxyl or amino group. When the product has a nitro group, this group may be converted into an amino group by reducing it by an ordinary method of reducing nitro groups, such as catalytic reduction conducted in the presence of a palladium/carbon catalyst or a method wherein zinc powder and hydrochloric acid are used.

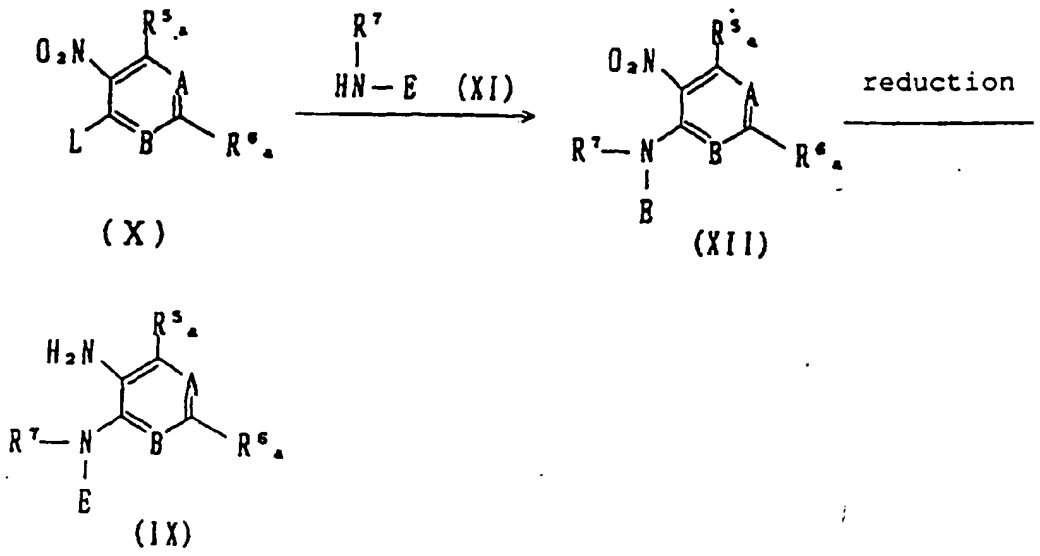
Next the description will be made on the processes for producing the starting compounds (IX) used in the present invention:



(IX)

wherein R^5_a, R^6_a, R^7, A, B and E are each as defined above or salts of them.

Production process 1

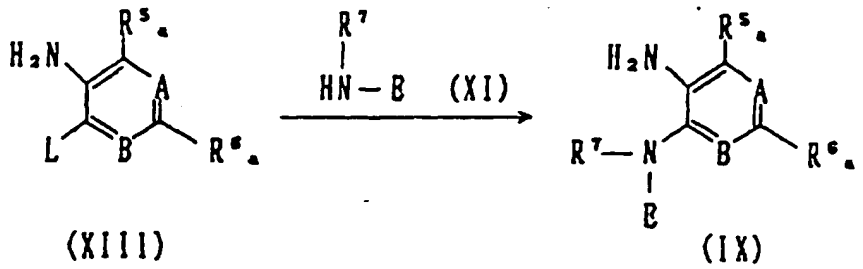


wherein L represents a halogen atom and R^5_a, R^6_a, R^7, A, B and E are each as defined above.

The compounds of the general formula (XII) can be synthesized by various processes described in publications such as J. Med. Chem., Vol. 21, p. 965, J. Org. Chem., Vol. 28, p. 3114, J. Chem. Soc. Perkin I, 1974, 1611, 1974, 1970 and 1979, 135, Helv. Chim. Acta, Vol. 61, p. 2452 or processes analogous to them. Namely, they can be produced by reacting a compound of the general formula (X) with a compound of the general formula (XI) in the presence or absence of an organic solvent such as dimethylformamide, ethanol or dioxane at room temperature or under heating.

When it is desired to remove a hydrogen halide thus formed, an organic base such as triethylamine or pyridine or an alkali carbonate is added as a acid binder or the reaction is conducted by using at least two equivalents of the compound (XI) per equivalent of the compound (X). When the product (XII) has a highly reactive halogen atom on its aromatic ring, it can be further reacted with an alkoxide or amine to convert it into another compound. The compound of the general formula (IX) can be obtained by reducing the compound (XII) produced as described above by an ordinary process for reducing nitro groups. In a preferred example of the reduction processes, catalytic reduction is conducted in the presence of a palladium/carbon catalyst or the reduction is conducted by using zinc powder and acetic acid. The catalytic reduction can be conducted usually in an organic solvent such as methanol, tetrahydrofuran or dimethylformamide under atmospheric or elevated pressure.

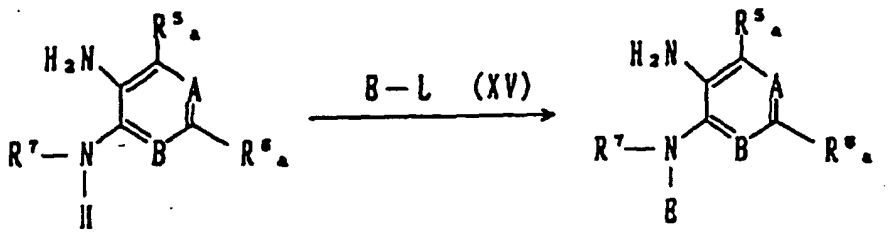
Production process 2



wherein R^5_a, R^6_a, R^7, A, B, E and L are each as defined above.

The compounds represented by the general formula (IX) can be synthesized by, for example, a process described in J. Org. Chem., Vol. 24, p. 1314, a process described in J. Heterocycl. Chem., Vol. 20, p. 1339, or a process analogous to them. Namely, they can be produced by reacting a compound of the general formula (XIII) with a compound of the general formula (XI) in the presence of an acid catalyst such as hydrochloric acid or sulfuric acid in a solvent such as water, ethanol or diethylene glycol. For increasing the reaction velocity, it is advantageous to heat the reaction mixture.

Production process 3

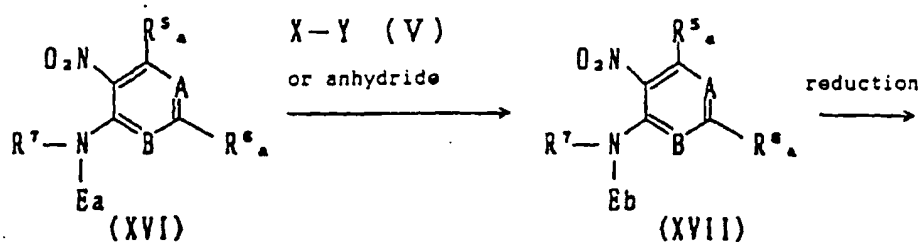


(XIV) (IX)

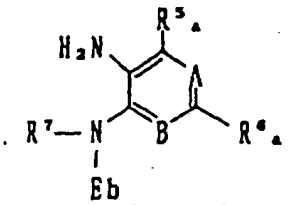
wherein R^5_a, R^6_a, R^7, A, B, E and L are each as defined above.

The compounds represented by the general formula (IX) can be synthesized by, for example, a process described in J. Chem. Soc. (C) (1970), p. 1355 or a process analogous to it. Namely, they can be produced by reacting a compound of the general formula (XIV) with a compound of the general formula (XV) in the presence or absence of an organic solvent such as dimethylformamide or dioxane at room temperature or under heating.

Production process 4



(XVI) (XVII)



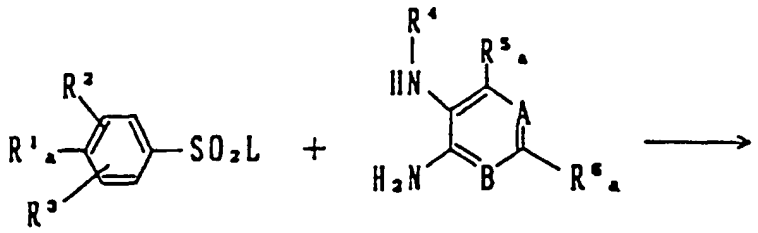
(XVIII)

wherein R^5_a, R^6_a, R^7, A, B and Ea are each as defined above and Eb represents E defined above in which at least one G is a protected hydroxyl group.

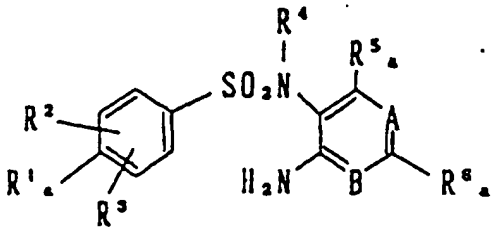
The compounds represented by the general formula (XVII) can be produced by reacting a compound of the general formula (XVI) with a compound of the general formula: X-Y (V) wherein X and Y are as defined above or with an inorganic acid or organic acid anhydride reactive with the hydroxyl group. The reaction conditions vary depending on

the varieties of X-Y (V) and the anhydride. The reaction solvent is usually preferably an inert solvent which is not reactive with these compounds, such as dimethylformamide, tetrahydrofuran or dioxane. To increase the reaction velocity, a base such as sodium hydride, potassium carbonate or triethylamine may be added to the reaction system or the reaction system may be heated. When R^7 is a hydrogen atom, it is sometimes preferred to protect it with an ordinary amino-protective group such as a benzyloxycarbonyl group prior to the reaction with X-Y (V) or the anhydride and to remove the protective group after the completion of the reaction. The compounds represented by the general formula (XVIII) can be produced by reducing the compounds (XVII) produced as described above by an ordinary process for reducing nitro groups.

Production process 5



(XIX) (XX)



(VII)

wherein R^1_a, R^2, R^3, R^4, R^5_a, R^6_a, A, B and L are each as defined above.

The compounds represented by the general formula (VII) can be produced by reacting a compound of the general formula (XIX) with a compound of the general formula (XX). The reaction conditions vary depending on the compounds. Usually 2 to 4 equivalents of the compound (XX) is preferably used per equivalent of the sulfonyl halide (XIX). The reaction solvent is preferably tetrahydrofuran, dioxane, pyridine, dimethylformamide or the like. The reaction can be conducted also under hydrous conditions. The reaction usually proceeds at room temperature and, if desired it may be conducted under cooling or heating.

When the compounds of the present invention are used as medicines, they are given by oral or parenteral administration. The dosage is not limited, since it varies depending on the symptoms; age, sex, body weight and sensitivity of the patient; administration method; time and interval of administration; properties, formulation and kind of the preparation; and the variety of the active ingredient.

The dose which varies depending on the administration manner is usually 10 to 6000 mg, preferably about 50 to 4000 mg and still preferably 100 to 3000 mg a day for adult. This dose of the compound is given in portions 1 to 3 times a day.

In the production of a solid preparation for oral administration, an excipient and, if necessary, binder, disintegrator, lubricant, colorant, corrigent, etc., are added to the active ingredient and they are shaped into tablets, coated tablets, granules, fine granules, powder or capsules.

Examples of the excipients include lactose, corn starch, white sugar, glucose, sorbitol, crystalline cellulose and silicon dioxide. Examples of the binders include polyvinyl alcohol, polyvinyl ether, ethylcellulose, methylcellulose, acacia, tragacanth, gelatin, shellac, hydroxypropylcellulose, hydroxypropylmethylcellulose, calcium citrate, dextrin and pectin. Examples of the lubricants include magnesium stearate, talc, polyethylene glycol, silica and hardened vegetable oils. The colorants are those admitted to be added to medicines. Examples of the corrigents include cocoa powder, methanol, aromatic powder, peppermint oil, borneol and cinnamon powder. These tablets and granules may be suitably coated with sugar, gelatin or the like, as a matter of course.

In the preparation of an injection, a pH modifier, buffering agent, suspending agent, solubilizer, stabilizer, isotonizer, preservative, etc., are added to the active ingredient to form an intravenous, subcutaneous or intramuscular injection by an ordinary process. If necessary, they are freeze-dried.

Examples of the suspending agents include methylcellulose, Polysorbate 80, hydroxyethylcellulose, acacia, tragacanth powder, sodium carboxymethylcellulose and polyoxyethylene sorbitan monolaurate.

Examples of the solubilizers include polyoxyethylene-hardened castor oil, Polysorbate 80, nicotinamide, polyoxyethylene sorbitan monolaurate, macrogol and ethyl esters of castor oil fatty acids.

Examples of the stabilizers include sodium sulfite, sodium metasulfite and ether. Examples of the preservatives include methyl p-hydroxybenzoate, ethyl p-hydroxybenzoate, sorbic acid, phenol, cresol and chlorocresol.

Effect of the Invention

The following pharmacological experiments will illustrate the effects of the compounds of the present invention.

Experimental Example 1

In vitro antineoplastic test on KB cells (human nasopharyngeal cells):

1.25×10^3 (0.1 mℓ) of KB cells suspended in a RPMI 1640 medium (a product of Nissui Seiyaku Co., Ltd.) containing 20% of bovine fetus serum, penicillin (100 units/ml), streptomycin (100 μg/ml), mercaptoethanol (5×10^{-5} M) and sodium pyruvate (1 mM) were placed in each hole of a 96-hole flat-bottom microplate and cultured in an incubator containing 5% of carbon dioxide at 37°C for one day.

A compound of the present invention was dissolved in dimethyl sulfoxide to obtain a 20 mg/ml solution, which was diluted to a concentration of 100 μg/ml with 0.1% bovine fetus serum/RPMI 1640 culture liquid. This concentration was the maximum one, which was subjected to two-fold serial dilution with 0.1% bovine fetus serum RPMI 1640 culture liquid containing 0.5% of dimethyl sulfoxide. It was added to the KB cells in each hole of the above-described culture plate in an amount of 0.1 ml and cultured in an incubator containing 5% of carbon dioxide at 37°C for three days.

After the completion of the culture, 0.05 ml of MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] solution (3.3 mg/ml) was added to each hole and the culture was conducted for additional 1 h. The supernatant liquid was removed from each hole by suction and a formazan thus formed was dissolved in 0.1 ml of dimethyl sulfoxide. The absorbance at 540 nm was determined with a microplate reader to use as an index of a viable count. A percentage inhibition was calculated according to the following formula and the concentration of the test compound for 50% inhibition (IC_{50}) was determined.

$$\text{Percentage inhibition (\%)} = (C-T)/C \times 100$$

T: absorbance of the hole containing the test compound
C: absorbance of the hole containing no test compound

Values of IC_{50} thus determined are given in Table 1.

Table 1

Compound (Ex. No.)	IC_{50} (μg/ml)	Compound (Ex. No.)	IC_{50} (μg/ml)
1	1.5	54	0.54
2	1.7	57	0.17
3	0.27	58	1.2
4	1.9	59	0.18
5	0.73	61	0.83
6	0.42	62	0.53
7	1.0	63	0.20
8	0.89	64	0.55
9	0.34	65	0.20
10	0.21	67	1.4
11	0.33	68	0.17
13	2.6	70	0.033

Table 1 (continued)

Compound (Ex. No.)	IC_{50} (μg/ml)	Compound (Ex. No.)	IC_{50} (μg/ml)
16	1.5	71	0.11
17	0.94	72	0.012
18	0.73	76	0.13
21	1.1	82	0.026
27	1.4	85	0.010
34	0.11	88	0.010
35	0.45	91	0.079
36	0.72	94	0.064
37	1.3	95	0.045
40	2.1	97	0.15
42	0.59	98	0.079
43	0.26	101	0.10
47	2.6	104	0.099
52	0.54	106	0.30

Experimental Example 2

In vivo antineoplastic test on colon 38 (cancer of the colon of mice):

About 75 mg of colon 38 was subcutaneously transplanted in the side of the body of each of 7-week old female BDF_1 mice. A compound of the present invention was suspended in 0.5% methylcellulose and oral admistration of a predetermined amount of the suspension once a day was started on the next day and continued for 8 days. 0.5% methylcellulose was orally given to a control group. The control group consisted of 10 mice and the group to which the medicine was given consisted of 6 mice.

21 days after the transplantation, the tumors were taken out and weighed. The tumor growth inhibition ratio of the group to which the medicine was given to the control group was determined according to the following formula:

$$\text{Growth inhibition ratio (\%)} \quad (C-T)/C \times 100$$

T: average weight of tumor in the group to which the test compound was given
C: average weight of tumor in the control group

The results of the experiments are given in Table 2.

Table 2

Compound (Ex. No.)	Dose (mg/kg/day)	Growth inhibition ratio	Survival rate on the day of judgement (the 21st day)
1	100	80	100
2	100	69	100
3	100	98	100
4	100	99	100
6	100	98	100
7	50	61	100
70	50	63	100

Experimental Example 3: Toxicity tests

A 0.5% suspension of a compound of Example 3, 4 or 6 in methylcellulose was given to a group of five 7-week old female BDF_1 mice once and the viability of them was observed for 7 days after the administration. No mouse died even with 1651 mg/kg of the compound.

It is apparent from the above Experimental Examples that the compounds of the present invention have a quite excellent antineoplastic effect. In addition, the compounds of the present invention have such a high safety that they

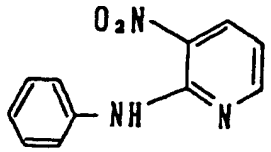
are useful as a remedy for malignant tumors, i.e. as an antineoplastic agent.

Examples

The following Production Examples will illustrate the processes for producing the starting compounds of the compounds of the present invention and the following Examples will illustrate the typical compounds of the present invention, which by no means limit the invention.

Production Example 1

2-Anilino-3-nitropyridine:

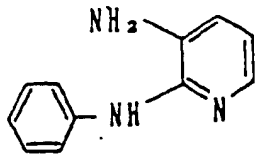


A mixture of 11.21 g (70 mmol) of 2-chloro-3-nitropyridine and 19.56 g (210 mmol) of aniline was heated under stirring at 100°C for 1 h. The reaction liquid was cooled to room temperature and dissolved in ethyl acetate. The solution was washed with an aqueous citric acid solution and then with water. After drying over magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was recrystallized from ethyl acetate/n-hexane to obtain 13.7 g of the title compound.
Melting point: 73 to 74°C
FAB mass spectrometry m/z: 216 ($[M+H]^+$)
^{1}H-NMR ($CDCl_3$) δ (ppm):
6.84 (1H, dd, J=8.4, 4.4Hz), 7.18-7.22 (1H, m), 7.37-7.43 (2H, m), 7.62-7.68 (2H, m), 8.49 (1H, dd, J=4.4, 2.0Hz), 8.53 (1H, dd, J=8.4, 2.0Hz), 10.12 (1H, br-s)

Elementary analysis for $C_{11}H_9N_3O_2$:			
	C	H	N
Calculated	61.39	4.22	19.53
Found	61.49	4.34	19.23

Production Example 2

3-Amino-2-anilinopyridine:



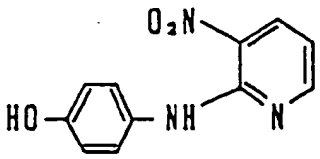
6.8 g (31.6 mmol) of the compound produced in Production Example 1 was dissolved in a mixture of 40 ml of tetrahydrofuran and 6 ml of methanol. Palladium/carbon was added to the solution to conduct hydrogenation at room temperate under atmospheric pressure. The palladium/carbon was removed by filtration, the solvent was distilled off under reduced pressure and the residue was recrystallized from ethyl acetate/n-hexane to obtain 5.5 g of the title compound.

Melting point: 143 to 144°C
FAB mass spectrometry m/z: 186 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 4.95-5.10 (2H, br), 6.61 (1H, dd, J=7.2, 4.8Hz), 6.80-6.86 (1H, m), 6.90 (1H, dd, J=7.2, 1.6Hz), 7.18-7.24 (2H, m), 7.49 (1H, dd, J=4.8, 1.6Hz), 7.60-7.65 (2H, m), 7.69 (1H, s)

Elementary analysis for $C_{11}H_{11}N_3$:			
	C	H	N
Calculated	71.33	5.99	22.69
Found	71.49	6.04	22.59

Production Example 3

4-[(3-Nitro-2-pyridyl)amino]phenol



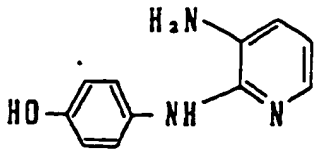
8.17 g (50 mmol) of 2-chloro-3-nitropyridine and 16.70 g (150 mmol) of p-aminophenol were added to 50 ml of dimethylformamide and the mixture was stirred at 100°C for 40 min. The solvent was distilled off under reduced pressure, the same treatment as that of Production Example 1 was repeated and the product was recrystallized from ethanol to obtain 9.4 g of the title compound.

Melting point: 143 to 144°C
FAB mass spectrometry m/z: 231 (M$^+$)
^{1}H-NMR ($CDCl_3$) δ (ppm): 5.23 (1H, s), 6.79 (1H, dd, J=4.8, 8.4Hz), 6.84 (2H, d, J=8.8Hz), 7.41 (2H, d, J=8.8Hz), 8.44 (1H, dd, J=1.6, 4.8Hz), 8.52 (1H, dd, J=1.6, 8.4Hz), 9.94 (1H, br-s)

Elementary analysis for $C_{11}H_9N_3O_3$:			
	C	H	N
Calculated	57.14	3.92	18.18
Found	57.15	3.97	18.14

Production Example 4

4-[(3-Amino-2-pyridyl)amino]phenol



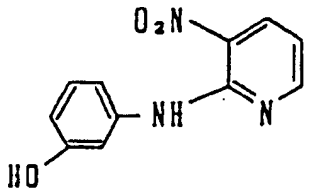
9.25 g (40 mmol) of the compound produced in Production Example 3 was catalytically reduced and treated in the same manner as that of Production Example 2 and the product was recrystallized from methanol to obtain 7.8 g of the title compound.

Melting point: 205 to 207°C
FAB mass spectrometry m/z: 202 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 4.94 (2H, br-s), 6.50 (1H, dd, J=4.8, 7.6Hz), 6.66 (2H, d, J=8.8Hz), 6.82 (1H, dd, J=1.6, 7.6Hz) 7.38 (1H, s), 7.39 (2H, d, J=8.8Hz), 7.40 (1H, dd, J=1.6, 4.8Hz), 8.85 (1H, s)

Elementary analysis for $C_{11}H_{11}N_3O$:			
	C	H	N
Calculated	65.66	5.51	20.88
Found	65.85	5.51	20.84

Production Example 5

3-[(3-Nitro-2-pyridyl)amino)]phenol:

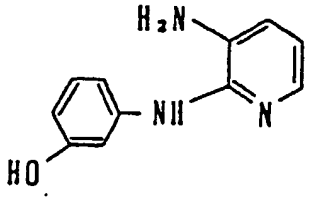


Melting point: 148 to 149°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 232 ([M+H]+)
^{1}H-NMR ($CDCl_3$) δ (ppm): 5.31 (1H, br-s), 6.65 (1H, dd, J=8.0, 2.4Hz), 6.85 (1H, dd, J=8.4, 4.8Hz), 7.08(1H, dd, J=8.0, 2.4Hz), 7.24 (1H, t, J=8.0Hz), 7.37 (1H, t, J=2.4Hz), 8.49 (1H, dd, J=4.8, 1.6Hz), 8.54 (1H, dd, J=8.4, 1.6Hz), 10.11 (1H, br-s)

Elementary analysis for $C_{11}H_9N_3O_3$:			
	C	H	N
Calculated	57.14	3.92	18.17
Found	57.33	4.03	18.18

Production Example 6

3-[(3-Amino-2-pyridyl)amino)]phenol:



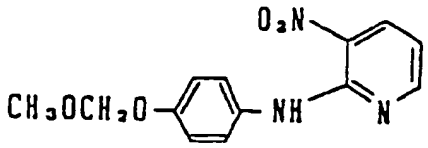
Melting point: gradual decomposition observed at 198°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 202 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 5.04 (2H, s), 6.24-6.28 (1H, m), 6.60 (1H, dd, J=7.6, 4.8Hz), 6.89 (1H, dd, J=7.6, 1.6Hz), 6.97-6.99 (2H, m), 7.23 (1H, br-s), 7.50 (1H, dd, J=4.8,

1.6Hz), 7.57 (1H, s), 9.10 (1H, s)

Elementary analysis for $C_{11}H_{11}N_3O$:			
	C	H	N
Calculated	65.66	5.51	20.88
Found	65.92	5.58	20.86

Production Example 7

2-[(4-Methoxymethyloxyphenyl)amino]-3-nitpopyridine



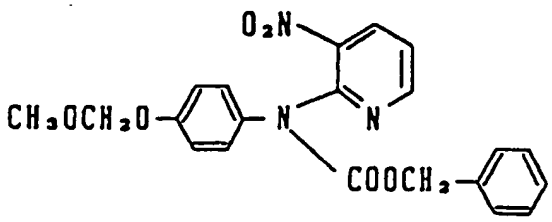
8.4 g (54.8 mmol) of 4-methoxymethyloxyaniline and 7.5 g (49 mmol) of 2-chloro-3-nitropyridine were dissolved in 35 ml of dimethylformamide. 7.6 g (55 mmol) of anhydrous potassium carbonate was added to the solution. The resulting solution was heated under stirring at 100°C for 4 h. The reaction liquid was cooled to room temperature and an insoluble matter thus formed was removed by filtration. The solvent was distilled off under reduced pressure and the residue was dissolved in ethyl acetate. The solution was washed with an aqueous citric acid solution and then with water. After drying over magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was recrystallized from ethanol to obtain 9.68 g of the title compound.

Melting point: 80 to 81°C
FAB mass spectrometry m/z: 275 (M^+)
^{1}H-NMR ($CDCl_3$) δ (ppm): 3.50 (3H, s), 5.19 (2H, s), 6.79 (1H, dd, J=4.4, 8.4Hz), 7.08 (2H, d, J=8.8Hz), 7.50(2H, d, J=8.8Hz), 8.45 (1H, dd, J=1.6, 4.4Hz), 8.51 (1H, dd, J=1.6, 8.4Hz), 9.99 (1H, br-s)

Elementary analysis for $C_{13}H_{13}N_3O_4$:			
	C	H	N
Calculated	56.73	4.76	15.27
Found	57.06	4.83	15.02

Production Example 8

2-[N-Benzyloxycarbonyl-N-(4-methoxymethyloxyphenyl)amino]-3-nitropyridine:



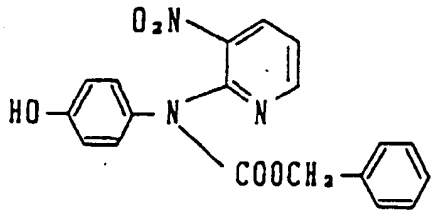
4.0 g (14.5 mmol) of the compound produced in Production Example 7 was dissolved in 70 ml of dimethylformamide.

720 mg (18 mmol) of sodium hydride (60%) was added to the solution. 3.2 ml (22.4 mmol) of benzyl chloroformate was added dropwise thereto under stirring at room temperature. After stirring at room temperature overnight, the solvent was distilled off under reduced pressure. Ethyl acetate and water were added to the residue and the ethyl acetate layer was separated. After washing the separated layer with water followed by drying (over magnesium sulfate), concentration and purification by silica gel column chromatography, 4.5 g of an oily title compound was obtained.

^{1}H-NMR ($CDCl_3$) δ (ppm): 3.47 (3H, s), 5.17 (4H, s+s), 7.06 (2H, d, J=8.8Hz), 7.22-7.26 (2H, m), 7.29-7.33 (4H, m), 7.37 (2H, d, J=8.8Hz), 8.29 (1H, d, J=8.0Hz), 8.56 (1H, d, J=4.4Hz)

Production Example 9

4-[N-Benzyloxycarbonyl-N-(3-nitro-2-pyridyl)amino]phenol:

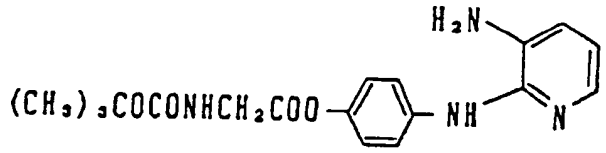


500 mg (1.22 mmol) of the compound produced in Production Example 8 was dissolved in a mixture of 6 ml of tetrahydrofuran and 1 ml of water. 2 ml of concentrated hydrochloric acid was added to the solution. After the mixture was stirred at room temperature overnight, the solvent was distilled off under reduced pressure. Ethyl acetate and a saturated aqueous sodium hydrogencarbonate solution were added to the residue and the ethyl acetate layer thus formed was separated. After washing the separated layer with water followed by drying (over magnesium sulfate) and concentration, 445 mg of the title compound was obtained.

^{1}H-NMR (DMSO-d_6) δ (ppm): 5.11 (2H, s), 6.77 (2H, d, J=8.8Hz), 7.18-7.24 (4H, m), 7.31-7.34 (3H, m), 7.58 (1H, dd, J=4.8, 8.0Hz), 8.51 (1H, dd, J=1.6, 8.0Hz), 8.66 (1H, dd, J=1.6, 4.8Hz), 9.64 (1H, s)

Production Example 10

4-[(3-Amino-2-pyridyl)amino]phenyl tert-butoxycarbonylaminoacetate:



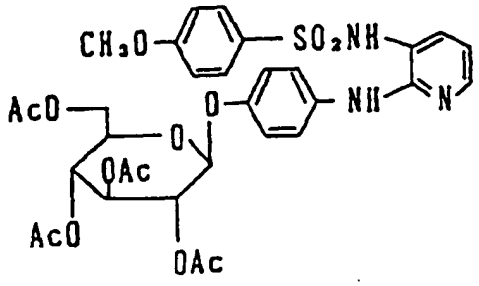
440 mg (1.2 mmol) of the compound produced in Production Example 9, 250 mg (1.43 mmol) of N-(tertbutoxycarbonyl)glycine and 25 mg (0.2 mmol) of 4-dimethylaminopyridine were dissolved in 10 ml of pyridine. 290 mg (1.41 mmol) of 1,3-dicyclohexylcarbodiimide was added to the solution. After stirring at room temperature overnight, the solvent was distilled off under reduced pressure. Ethyl acetate was added to the residue, the insoluble matter was removed by filtration and the solvent was distilled off under reduced pressure. The residue was purified according to silica gel column chromatography and the resulting compound was catalytically reduced in the presence of a palladium/carbon catalyst by an ordinary process. After the removal of the catalyst by filtration followed by concentration, the residue was purified by silica gel column chromatography to obtain 236 mg of the title compound.

^{1}H-NMR (DMSO-d_6) δ (ppm): 1.41 (9H, s), 3.93 (2H, d, J=6.0Hz), 5.05 (2H, br-s), 6.62 (1H, dd, J=4.8,

7.2Hz), 6.90 (1H, dd, J=1.6, 7.2Hz), 6.96 (2H, d, J=9.2Hz), 7.37 (1H, br-t, J=6.4Hz), 7.49 (1H, dd, J=1.6, 4.8Hz), 7.64 (2H, d, J=9.2Hz), 7.79 (1H, s)

Production Example 11

4-[[3-(4-Methoxybenzenesulfonamido)-2-pyridyl]amino]phenyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside:

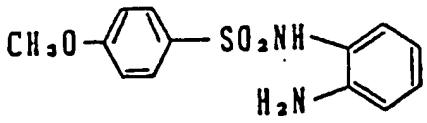


3.753 g (10.10 mmol) of the compound produced in Example 6 and 3.959 g (10.14 mmol) of β-D-glucose pentaacetate were suspended in 200 ml of 1,2-dichloroethane. 30 ml of a 1.0 M solution of tin tetrachloride in dichloromethane was added dropwise to the suspension under stirring and under cooling with ice in a nitrogen atmosphere. After stirring under cooling with ice for 2 h and then at room temperature for 4 days, the reaction mixture was added to ice/water containing 16 g of sodium hydrogencarbonate. The organic solvent was distilled off under reduced pressure. Ethyl acetate was added to the residue and the insoluble matter thus formed was removed by filtration. The ethyl acetate layer was separated, washed with water, dried, concentrated and purified by silica gel column chromatography to obtain 2.47 g of the title compound.

^{1}H-NMR ($CDCl_3$) δ (ppm): 2.04 (3H, s), 2.05 (3H, s), 2.08 (3H, s), 2.10 (3H, s), 3.80-3.86 (1H, m), 3.84 (3H, s), 4.17 (1H, dd, J=12.4, 2.4Hz), 4.30 (1H, dd, J=12.4, 5.6Hz), 4.99 (1H, d, J=7.6Hz), 5.16 (1H, t, J=9.6Hz), 5.23-5.32 (2H, m), 6.37 (1H, br-s), 6.54 (1H, dd, J=4.8, 7.6Hz), 6.84 (1H, dd, J=1.6, 7.6Hz), 6.92 (2H, d, J=8.8Hz), 6.94 (2H, d, J=8.8Hz), 7.32 (1H, br-s), 7.38 (2H, d, J=8.8Hz), 7.69 (2H, d, J=8.8Hz), 8.07 (1H, dd, J=1.6, 4.8Hz)

Production Example 12

N-(2-Aminophenyl)-4-Methoxybenzenesulfonamide:



33.1 g (0.3 mol) of 1,2-phenylenediamine was dissolved in 200 ml of dioxane. A solution of 20.87 g (0.1 mol) of 4-methoxybenzenesulfonyl chloride in 110 ml of dioxane was added thereto under stirring. The resulting mixture was stirred at room temperature overnight. 12.1 g (0.12 mol) of triethylamine was added thereto. After concentration followed by addition of an aqueous citric acid solution and ethyl acetate, the organic layer was separated, concentrated and purified by silica gel column chromatography to obtain 27.1 g of the title compound.

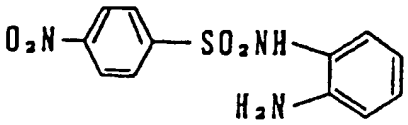
Melting point: 141 to 142°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 279 ([M+H]$^+$)
^{1}H-NMR(DMSO-D_6)δ(ppm): 3.81 (3H, s), 4.91 (2H, br-s), 6.37 (1H, td, J=1.6, 7.2, 8.0Hz), 6.60 (1H, dd, J=1.6, 8.0Hz), 6.66 (1H, dd, J=1.6, 8.0Hz), 6.86 (1H, td, J=1.6, 7.2, 8.0Hz),

7.03 (2H, d, J=8.8Hz), 7.61 (2H, d, J=8.8Hz), 9.07 (1H, br-s)

Elementary analysis for $C_{13}H_{14}N_2O_3S$:			
	C	H	N
Calculated	56.10	5.07	10.07
Found	55.98	5.03	10.00

Production Example 13

N-(2-Aminophenyl)-4-nitrobenzenesulfonamide:



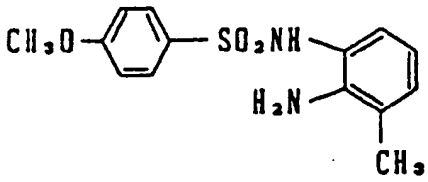
The title compound was produced in the same manner as that of Production Example 12.

Melting point: 190 to 191°C (recrystallized from benzene)
FAB mass spectrometry m/z: 294 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ(ppm): 4.90 (2H, br-s), 6.42 (1H, dt, J=1.6, 8.0Hz), 6.61 (1H, dd, J=1.6, 8.0Hz), 6.71 (1H, dd, J=1.6, 8.0Hz), 6.91 (1H, dt, J=1.6, 8.0Hz), 7.91 (2H, d, J=8.8Hz), 8.36 (2H, d, J=8.8Hz)

Elementary analysis for $C_{12}H_{11}N_3O_4S$:			
	C	H	N
Calculated	49.14	3.78	14.33
Found	49.38	3.82	14.13

Production Example 14

N- (2-Amino-3-methylphenyl) -4-methoxybenzenesulfonamide:



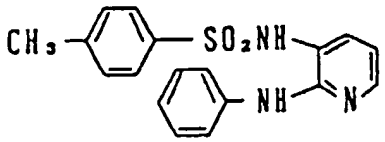
The title compound was produced in the same manner as that of Production Example 12.

Melting point: 177 to 178°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 293 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 2.03 (3H, s), 3.81 (3H, s), 4.75 (2H, br-s), 6.30 (1H, t, J=7.6Hz), 6.44 (1H, dd, J=1.2, 7.6Hz), 6.79 (1H, dd, J=1.2, 7.6Hz), 7.04 (2H, d, J=8.8Hz), 7.61 (2H, d, J=8.8Hz)

Elementary analysis for $C_{14}H_{16}N_2O_3S$:			
	C	H	N
Calculated	57.52	5.52	9.58
Found	57.76	5.51	9.57

Example 1

N-(2-Anilino-3-pyridyl)-p-toluenesulfonamide:



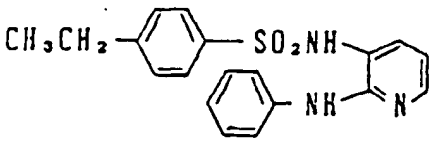
3.7g (20 mmol) of the compound produced in Production Example 2 was dissolved in 30 ml of pyridine. 30 ml of a solution of 3.81 g (20 mmol) of p-toluenesulfonyl chloride in tetrahydrofuran was added in portions to the solution under stirring at room temperature. After stirring overnight, the solvent was distilled off under reduced pressure and the residue was dissolved in ethyl acetate. The solution was washed with water and dried over magnesium sulfate. The solvent was distilled off under reduced pressure and the residue was recrystallized from ethanol to obtain 5.2 g of the title compound.

Melting point: 164 to 165°C
FAB mass spectrometry m/z: 340 ([M+H]+]
^{1}H-NMR (DMSO-d_6) δ (ppm): 2.23 (3H, s), 6.73 (1H, dd, J=4.8, 7.6 Hz), 6.86-6.92 (1H, m), 7.18-7.24 (2H, m), 7.24 (2H, d, J =8.0Hz), 7.27 (1H, dd, J=7.6, 1.6Hz), 7.36-7.42 (2H, m), 7.54 (2H, d, J=8.0Hz), 7.86 (1H, s), 7.99 (1H, dd, J=4.8, 1.6Hz), 9.62 (1H, s)

Elementary analysis for $C_{18}H_{17}N_3O_2S$:			
	C	H	N
Calculated	63.70	5.05	12.38
Found	63.77	5.11	12.28

Example 2

N-(2-Anilino-3-pyridyl)-4-ethylbenzenesulfonamide:



3.11 g (16.8 mmol) of the compound produced in Production Example 2 was reacted with 3.43 g (16.8 mmol) of p-ethylbenzenesulfonyl chloride and the product was treated in the same manner as that of Example 1 to obtain 5.0 g of the title compound.

Melting point: 138 to 139°C (recrystallized from ethanol)

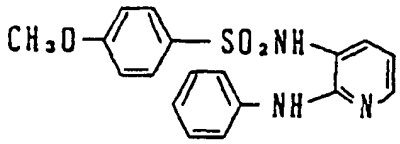
FAB mass spectrometry m/z: 354 ([M+H]$^+$)

^{1}H-NMR (DMSO-d_6) δ (ppm): 1.02 (3H, t), 2.50 (2H, q), 6.72 (1H, dd, J=5.2, 8.0Hz), 6.83-6.89 (1H, m), 7.14-7.20 (2H, m), 7.24 (2H, d, J=8.4Hz), 7.29 (1H, dd, J=8.0, 1.8Hz), 7.32-7.37 (2H, m), 7.54 (2H, d, J=8.4 Hz), 7.80 (1H, s), 7.97 (1H, dd, J=5.2, 1.8Hz), 9.60 (1H, s)

Elementary analysis for $C_{19}H_{19}N_3O_2S$:			
	C	H	N
Calculated	64.57	5.42	11.89
Found	64.89	5.33	12.00

Example 3

N-(2-Anilino-3-pyridyl)-4-methoxybenzenesulfonamide:



[0140]

1.39 g (7.5 mmol) of the compound produced in Production Example 2 was reacted with 1.55 g (7.5 mmol) of p-methoxybenzenesulfonyl chloride and the product was treated in the same manner as that of Example 1 to obtain 2.6 g of the title compound.

Melting point: 172 to 173°C (recrystallized from ethanol)

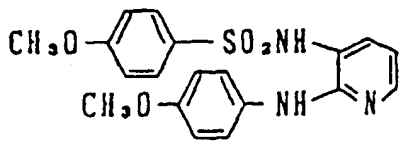
FAB mass spectrometry m/z: 356 ([M+H]$^+$)

^{1}H-NMR (DMSO-d_6) δ (ppm): 3.68 (3H, s), 6.71 (1H, dd, J=7.6, 5.0Hz), 6.84-6.90 (1H, m), 6.92 (2H, d, J=9.2Hz), 7.15-7.22 (2H, m), 7.25 (1H, dd, J= 7.6, 1.2Hz), 7.36-7.42 (2H, m), 7.57 (2H, d, J=9.2Hz), 7.86 (1H, s), 7.97 (1H, dd, J=5.0, 1.2Hz), 9.51 (1H, s)

Elementary analysis for $C_{18}H_{17}N_3O_3S$:			
	C	H	N
Calculated	60.83	4.82	11.82
Found	61.02	4.69	11.86

Example 4

4-Methoxy-N-[2-[(4-methoxyphenyl)amino]-3-pyridyl]benzenesulfonamide:

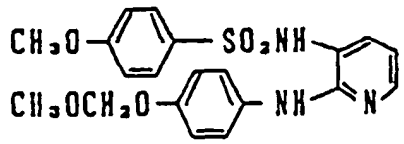


The title compound was obtained in the same manner as that of Example 1.

Melting point:	145 to 147°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	386 ([M+H]$^+$)
^{1}H-NMR ($CDCl_3$) δ (ppm):	3.79 (3H, s), 3.85 (3H, s), 6.16 (1H, br-s), 6.52 (1H, dd, J=4.8, 7.6Hz), 6.85 (3H, d, J=8.8Hz), 6.93 (2H, d, J=8.8Hz), 7.12 (1H, br-s), 7.32 (2H, d, J=8.8Hz), 7.69 (2H, d, J=8.8Hz), 8.07 (1H, dd, J=1.6,4.8Hz)

Example 5

4-Methoxy-N-[2-[(4-methoxymethyloxyphenyl)amino]-3-pyridyl]benzenesulfonamide:



Elementary analysis for $C_{19}H_{19}N_3O_4S$:			
	C	H	N
Calculated	59.21	4.97	10.90
Found	59.26	5.05	10.75

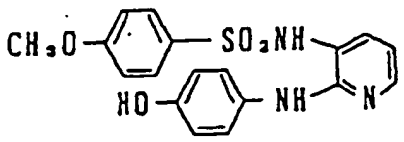
The title compound was produced in the same manner as that of Example 1.

Melting point:	118 to 119°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	416 ([M+H]$^+$)
^{1}H-NMR ($CDCl_3$) δ (ppm):	3.48 (3H, s), 3.83 (3H, s), 5.13 (2H, s), 6.45 (1H, br-s), 6.52 (1H, dd, J=4.4, 7.6 Hz), 6.87 (1H, dd, J=1.6, 7.6Hz), 6.92 (2H, d, J=8.8Hz), 6.97 (2H, d, J=8.8Hz), 7.16 (1H, br-s), 7.31 (2H, d, J=8.8Hz), 7.69 (2H, d, J=8.8Hz), 8.07 (1H, d)

Elementary analysis for $C_{20}H_{21}N_3O_5S$:			
	C	H	N
Calculated	57.82	5.09	10.11
Found	57.93	5.02	9.84

Example 6

N-[2-[(4-Hydroxyphenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



1.01 g (5 mmol) of the compound produced in Production Example 4 was reacted with 1.05 g (5 mmol) of p-

methoxybenzenesulfonyl chloride and the product was treated in the same manner as that of Example 1 to obtain 1.43 g of the title compound.

Melting point:	178 to 179°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	372 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.75 (3H, s), 6.60 (1H, dd, J=4.8, 7.6Hz), 6.63 (2H, d, J=8.8Hz), 6.98 (2H, d, J=8.8Hz), 7.14 (2H, d, J=8.8Hz), 7.18 (1H, dd, J=1.6, 7.6Hz), 7.58 (1H, br-s), 7.60 (2H, d, J=8.8Hz), 7.88 (1H, dd, J=1.6, 4.8Hz), 8.97 (1H, s), 9.44 (1H, s)

Elementary analysis for $C_{18}H_{17}N_3O_4S$:			
	C	H	N
Calculated	58.21	4.61	11.31
Found	58.40	4.67	11.38

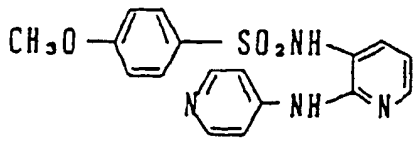
2.0 g of the title compound was dissolved in 50 ml of tetrahydrofuran. 0.5 ml of concentrated hydrochloric acid was added to the solution and the resulting solution was concentrated to dryness. The residue was recrystallized from methanol to obtain 1.9 g of hydrochloride of the title compound.

Melting point: gradual decomposition observed at 225°C.

Elementary analysis for $C_{18}H_{17}N_3O_4S \cdot HCl$:			
	C	H	N
Calculated:	53.01	4.45	10.30
Found:	52.97	4.33	10.19

Example 7

4-Methoxy-N-[2- [(4-pyridyl)amino]-3-pyridyl]-benzenesulfonamide:



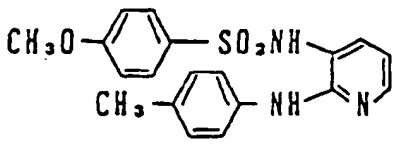
The title compound was produced in the same manner as that of Example 1.

Melting point:	172 to 173°C (recrystallized from ethyl acetate)
FAB mass spectrometry m/z:	357 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.67 (3H, s), 6.86-6.91 (3H, m), 7.37 (1H, dd, J=1.6, 7.6Hz), 7. 48 (2H, d, J=5.6Hz), 7.54 (2H, d, J=9.2Hz), 8.04 (1H, dd, J=1.6, 4.8Hz), 8.26 (2H, d, J=5.6Hz), 8.59 (1H, br-s)

Elementary analysis for $C_{17}H_{16}N_4O_3S$:			
	C	H	N
Calculated	57.29	4.53	15.72
Found	57.37	4.56	15.66

Example 8

4-Methoxy-N-[2-[(4-methylphenyl)amino]-3-pyridyl]benzenesulfonamide:



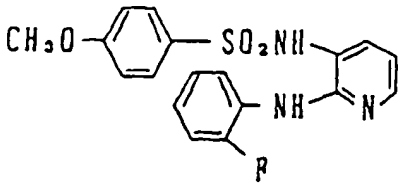
The title compound was produced in the same manner as that of Example 1.

Melting point: 188 to 189°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 370 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 2.21 (3H, s), 3.69 (3H, s), 6.66 (1H, dd, J=6.4, 2.4Hz), 6.92 (2H, d, J=7.2Hz), 6.99 (2H, d, J=7.6Hz), 7.21 (1H, dd, J=6.4, 1.6Hz), 7.27 (2H, d, J=7.2Hz), 7.56 (2H, d, J=7.6Hz), 7.75 (1H, s), 7.93 (1H, dd, J-2.4, 1.6Hz), 9.48 (1H, br-s)

Elementary analysis for $C_{19}H_{19}N_3O_3S$:			
	C	H	N
Calculated	61.77	5.18	11.38
Found	61.82	5.21	11.30

Example 9

N-[2-[(2-Fluorophenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



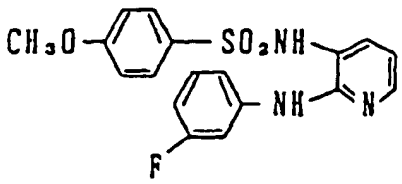
The title compound was produced in the same manner as that of Example 1.

Melting point: 148 to 150°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 374 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.72 (3H, s), 6.76 (1H, dd, J=7.6, 4.8Hz), 6.90-6.98 (3H, m), 7.05 (1H, td, J=8.0, 0.8Hz), 7.13-7.20 (2H, m), 7.57 (2H, d, J=8.8Hz), 7.82 (1H, d, J=2.8Hz), 7.95 (lH, t, J=8.0Hz), 8.01 (1H, dd, J=4.8, 1.6Hz), 9.76 (1H, s)

Elementary analysis for $C_{18}H_{16}FN_3O_3S$:			
	C	H	N
Calculated	57.90	4.32	11.25
Found	57.93	4.57	10.98

Example 10

N-[2-[(3-Fluorophenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



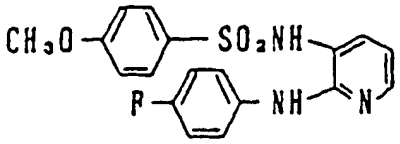
The title compound was produced in the same manner as that of Example 1.

Melting point:	180 to 181°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	374 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.69 (3H, s), 6.67 (1H, td, J=8.4, 2.0Hz), 6.81 (1H, dd, J=7.6, 4.8Hz), 6.92 (2H, d, J=8.8Hz), 7.09 (1H, dd, J=8.4, 2.0Hz), 7.22 (1H, dt, J=8.4, 6.8Hz), 7.31 (1H, dd, J=7.6, 1.6Hz), 7.49 (1H, dt, J=2.0, 12.4Hz), 7.56 (2H, d, J=8.8Hz), 8.05 (1H, dd, J=4.8, 1.6Hz), 8.12 (1H, s), 9.52 (1H, br-s)

Elementary analysis for $C_{18}H_{16}FN_3O_3S$:			
	C	H	N
Calculated	57.90	4.32	11.25
Found	57.89	4.42	11.16

Example 11

N-[2-[(4-Fluorophenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



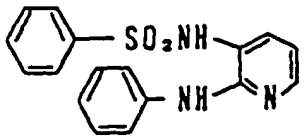
The title compound was produced in the same manner as that of Example 1.

Melting point:	196 to 197°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	374 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.71 (3H, s), 6.72 (1H, dd, J=4.8, 7.6Hz), 6.95 (2H, d, J=8.8Hz), 7.04 (2H, t, J=8.8Hz), 7.25 (1H, dd, J=1.6, 7.6Hz), 7.42 (2H, m), 7.58 (2H, d, J=8.8Hz), 7.95 (1H, br-s), 7.98 (1H, dd, J=1.6, 4.8Hz), 9.48 (1H, br-s)

Elementary analysis for $C_{18}H_{16}FN_3O_3S$:			
	C	H	N
Calculated	57.90	4.32	11.25
Found	57.83	4.32	11.21

Example 12

N-(2-Anilino-3-pyridyl)benzenesulfonamide:



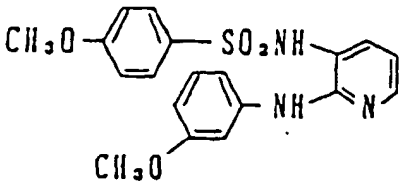
The title compound was produced in the same manner as that of Example 1.

Melting point: 148 to 150°C (recrystallized from methanol)
FAB mass spectrometry m/z: 326 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 6.73 (1H, dd, J=7.6, 4.8Hz), 6.87-6.93 (1H, m), 7.18-7.24 (2H, m), 7.25 (1H, dd, J=7.6, 1.6Hz), 7.41-7.47 (2H, m), 7.47-7.51 (2H, m), 7.51-7.57 (1H, m) 7.67-7.72 (2H, m), 7.90 (1H, s), 7.99 (1H, dd, J=4.8, 1.6Hz), 9.73 (1H, s)

Elementary analysis for $C_{17}H_{15}N_3O_2S$:			
	C	H	N
Calculated	62.75	4.65	12.91
Found	63.03	4.74	12.67

Example 13

4-Methoxy-N-[2-[(3-methoxyphenyl)amino]-3-pyridyl]benzenesulfonamide:



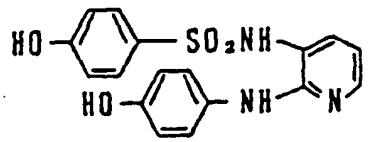
The title compound was produced in the same manner as that of Example 1.

Melting point: 161 to 162°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 386 ([M+H]$^+$)
^{1}H-NMR(DMSO-d_6) δ (ppm): 3.67, 3.70 (3H×2), 6.47 (1H, dd, J=8.0, 2.0Hz), 6.73 (1H, dd, J=8.0, 4.8Hz), 6.93 (2H, d, J=8.8Hz), 6.97 (1H, dd, J=8.0, 2.0Hz), 7.10 (1H, t, J=8.0Hz), 7.13 (1H, t, J=2.0Hz), 7.29 (1H, dd, J=8.0, 1.6Hz), 7.59 (2H, d, J=8.8Hz), 7.89 (1H, s), 8.01 (1H, dd, J=4.8, 1.6Hz), 9.55 (1H, s)

Elementary analysis for $C_{19}H_{19}N_3O_4S$:			
	C	H	N
Calculated	59.21	4.97	10.90
Found	59.14	4.96	10.74

Example 14

4-Hydroxy-N- [2-[(4-hydroxyphenyl)amino] -3-pyridyl] benzenesulfonamide:

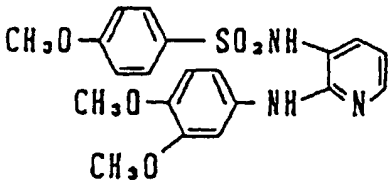


The compound produced in Example 4 was dissolved in DMF and five equivalents of sodium methanethiolate was added to the solution. The resulting solution was heated at 100°C and treated to obtain the title compound.

Melting point:	252 to 257°C (decomp.) (recrystallized from ethanol/water)
FAB mass spectrometry m/z:	358 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	6.60 (1H, dd, J=7.6, 4.8Hz), 6.65 (2H, d, J=8.8Hz), 6.81 (2H, d, J=8.8Hz), 7.14 (1H, dd, J=7.6, 1.6Hz), 7.19 (2H, d, J=8.8Hz), 7.52 (2H, d, J=8.8Hz), 7.61 (1H, s), 7.87 (1H, dd, J=4.8, 1.6Hz), 9.01 (1H, s), 9.39 (1H, s), 10.42 (1H, s)

Example 15

N-[2-[(3, 4-Dimethoxyphenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



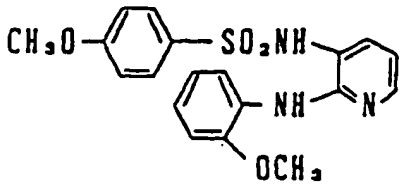
The title compound was produced in the same manner as that of Example 1.

Melting point:	126 to 127°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	415 (M$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.72, 3.73 (3H×3), 6.66 (1H, dd, J=8.0, 3.6Hz), 6.81 (1H, d, J=8.8Hz), 6.96-6.98 (3H, m), 7.02 (1H, s), 7.21 (1H, dd, J=8.0, 1.2Hz), 7.60 (2H, d, J=8.0Hz), 7.73 (1H, s), 7.95 (1H, dd, J=3.6, 1.2Hz), 9.45 (1H, br-s)

Elementary analysis for $C_{20}H_{21}N_3O_5S$:			
	C	H	N
Calculated	57.82	5.10	10.12
Found	57.73	5.10	10.07

Example 16

4-Methoxy-N-[2-[(2-methoxyphenyl)amino]-3-pyridyl]benzenesulfonamide:



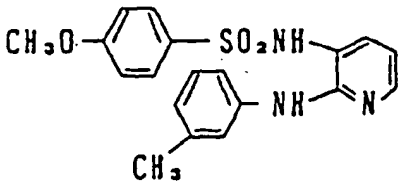
The title compound was produced in the same manner as that of Example 1.

Melting point: 159 to 160°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 386 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.78 (3H, s), 3.89 (3H, s), 6.69 (1H, dd, J=7.6, 4.8Hz), 6.87-6.90 (2H, m), 6.96-7.01 (2H, m), 7.05 (2H, d, J=8.8Hz), 7.66 (2H, d, J=8.8Hz), 8.08 (1H, dd, J=4.8, 1.6Hz), 8.10 (1H, s), 8.40 (1H, dd, J=6.4, 2.8Hz), 9.78 (1H, s)

Elementary analysis for $C_{19}H_{19}N_3O_4S$:			
	C	H	N
Calculated	59.21	4.97	10.90
Found	59.16	5.01	10.96

Example 17

4-Methoxy-N- [2-[(3-methyphenyl)amino] -3-pyridyl]-benzenesulfonamide:



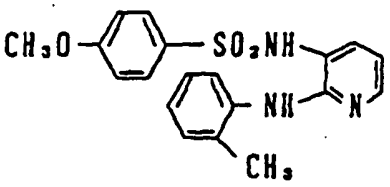
The title compound was produced in the same manner as that of Example 1.

Melting point: 147 to 148°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 370 ([M+H]+)
^{1}H-NMR(DMSO-d_6) δ (ppm): 2.26 (3H, s), 3.71 (3H, s), 6.71-6.73 (2H, m), 6.95 (2H, d, J=7.6Hz), 7.09 (1H, t, J=7.6Hz), 7.16 (1H, s), 7.25-7.27 (2H, m), 7.59 (2H, d, J=7.6Hz), 7.90 (1H, s), 8.00 (1H. dd, J=2.8, 1.6Hz), 9.53 (1H, br-s)

Elementary analysis for $C_{19}H_{19}N_3O_3S$:			
	C	H	N
Calculated	61.77	5.18	11.38
Found	61.79	5.18	11.46

Example 18

4-Methoxy-N-[2-[(2-methylphenyl)amino] -3-pyridyl] benzenesulfonamide:



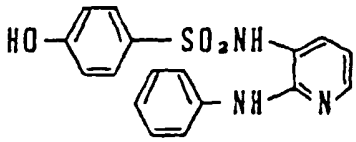
The title compound was produced in the same manner as that of Example 1.

Melting point:	147 to 148°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	370 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.06 (3H, s), 3.77 (3H, s), 6.65 (1H, dd, J=7.6, 4.8Hz), 6.92 (1H, t, J=7.6Hz), 7.03 (2H, d, J=8.8Hz), 7.09 (1H, t, J=7.6Hz), 7.11-7.15 (2H, m), 7.53 (1H, s), 7.55 (1H, d, J=7.6Hz), 7.63 (2H, d, J=8.8Hz), 7.91 (1H, dd, J=4.8, 1.6Hz), 9.67 (1H,s)

Elementary analysis for $C_{19}H_{19}N_3O_3S$:			
	C	H	N
Calculated	61.77	5.18	11.38
Found	61.80	5.17	11.40

Example 19

N- (2-Anilino-3-pyridyl) -4-hydroxybenzenesulfonamide:

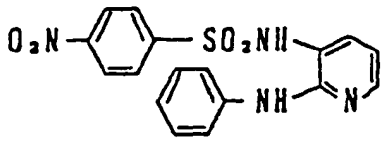


The title compound was produced by treating the compound of Example 3 in the same manner as that of Example 14.

Melting point:	226 to 228°C (recrystallized from methanol)
FAB mass spectrometry m/z:	342 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	6.71 (1H, dd, J=7.6, 4.8Hz), 6.79 (2H, d, J=8.8Hz), 6.88-6.94 (1H, m), 7.21 (1H, dd, J=7.6, 1.6Hz), 7.21-7.27 (2H, m), 7.46-7.51 (2H, m), 7.52 (2H, d, J=8.8Hz), 7.92 (1H, s), 7.97 (1H, dd, J=4.8, 1.6Hz), 9.50 (1H, s), 10.40 (1H, s)

Example 20

N-(2-Anilino-3-pyridyl)-4-nitrobenzenesulfonamide:



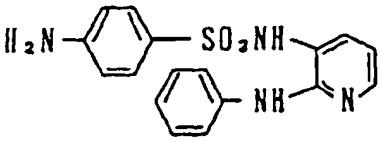
The title compound was produced in the same manner as that of Example 1.

Melting point: 191 to 192°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 371 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 6.80-6.83 (2H, m), 7.12 (2H, t, J=8.4Hz), 7.25 (2H, d, J=8.8Hz), 7.40 (1H, Dd, J=1.6, 7.6Hz), 7.83 (3H, d, J=8.8Hz), 8.07 (1H, br-s), 8.19 (2H, d, J=8.8Hz), 9.91 (1H, br-s)

Elementary analysis for $C_{17}H_{14}N_4O_4S$:			
	C	H	N
Calculated	55.13	3.81	15.13
Found	55.17	3.97	14.77

Example 21

4-Amino-N-(2-anilino-3-pyridyl)benzenesulfonamide:



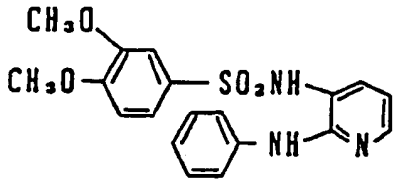
The title compound was produced by catalytically reducing the compound of Example 20 in the presence of a palladium/carbon catalyst by an ordinary process.

Melting point: 228 to 230°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 341 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 5.99 (2H, br-s), 6.50 (2H, d, J=8.8Hz), 6.70 (1H, dd, J=4.4, 7.6Hz), 6.91 (1H, td , J=0.8, 7.2Hz), 7.18 (1H, dd, J=1.6, 7.6 Hz), 7.24 (2H, t, J=7.6Hz), 7.33 (2H, d, J=8.8Hz), 7.53 (2H, dt, J=1.2, 7.6Hz), 7.95 (2H, br-s), 9.31 (1H, s)

Elementary analysis for $C_{17}H_{16}N_4O_2S$:			
	C	H	N
Calculated	59.98	4.74	16.46
Found	60.08	4.67	16.23

Example 22

N- (2-Anilino-3-pyridyl) -3,4-dimethoxybenzenesulfonamide:



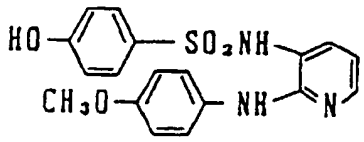
The title compound was produced in the same manner as that of Example 1.

Melting point: 171 to 172°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 386 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.64 (3H, s), 3.69 (3H, s), 6.75 (1H, dd, J=4.8, 7.6Hz),6.88 (1H, t, J=7.6Hz), 6.93 (1H, d, J=8.8Hz), 7.10 (1H, d, J=2.0Hz), 7.17-7.22 (3H, m), 7.32 (1H, d, J=7.6 Hz), 7.39 (2H, d, J=8.0Hz), 7.89 (1H, br-s), 8.00 (1H, d, J=4.8Hz), 9.48 (1H, br-s)

Elementary analysis for $C_{19}H_{19}N_3O_4S$:			
	C	H	N
Calculated:	59.21	4.97	10.90
Found:	59.22	4.91	10.63

Example 23

4-Hydroxy-N-[2-[(4-methoxyphenyl)amino]-3-pyridyl]-benzenesulfonamide:



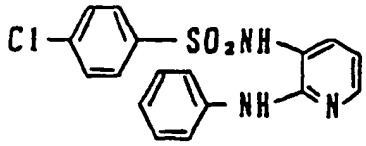
The title compound was produced by the same treatment as that of Example 14.

Melting point: 214 to 216°C (recrystallized from ethanol/water)
FAB mass spectrometry m/z: 372 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.71 (3H, s), 6.63 (1H, dd, J=7.6, 4.8Hz), 6.80 (2H, d, J=8.8Hz), 6.82 (2H, d, J=8.8Hz), 7.16 (1H, dd, J=7.6, 1.6Hz), 7.35 (2H, d, J=8.8Hz), 7.51 (2H, d, J=8.8Hz), 7.75 (1H, s), 7.90 (1H, dd, J=4.8, 1.6Hz), 9.41 (1H, s), 10.42 (1H, s)

Elementary analysis for $C_{18}H_{17}N_3O_4S$:			
	C	H	N
Calculated	58.21	4.61	11.31
Found	58.21	4.74	11.01

Example 24

N-(2-Anilino-3-pyridyl)-4-chlorobenzenesulfonamide:



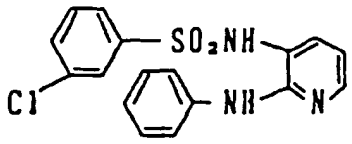
The title compound was produced in the same manner as that of Example 1.

Melting point:	186 to 188°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	360 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	6.77 (1H, dd, J=7.6, 4.8Hz), 6.90 (1H, dt, J=7.6, 0.8Hz), 7.22 (2H, t, J=7.6Hz), 7.30 (1H, dd, J=7.6, 1.2Hz), 7.38 (2H, dd, J=7.6, 0. 8Hz), 7.51 (2H, d, J=8.4Hz), 7.64 (2H, d, J=8.4Hz), 7.89 (1H, s), 8.02 (1H, dd, J=4.8, 1.2Hz), 9.76 (1H, br-s)

Elementary analysis for $C_{17}H_{14}ClN_3O_2S$:			
	C	H	N
Calculated	56.74	3.92	11.68
Found	56.79	4.03	11.67

Example 25

N-(2-Anilino-3-pyridyl)-3-chlorobenzenesulfonamide:



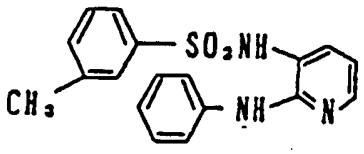
The title compound was produced in the same manner as that of Example 1.

Melting point:	143 to 144°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	360 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	6.77 (1H, dd, J=7.6, 4.8Hz), 6.91 (1H, dt, J=7.6, 1.2Hz), 7.21 (2H, t, J=7.6Hz), 7.32 (1H, dd, J=7.6, 1.6Hz), 7.41 (2H, dd, J=7.6, 1.2Hz), 7.46 (1H, t, J=8.0Hz), 7.54-7.61 (2H, m), 7.68 (1H, br-s), 7.92 (1H, br-s), 8.04 (1H, dd, J=4.8, 1.6Hz), 9.80 (1H, br-s)

Elementary analysis for $C_{17}H_{14}ClN_3O_2S$:			
	C	H	N
Calculated	56.74	3.92	11.68
Found	56.73	4.09	11.68

Example 26

N-(2-Anilino-3-pyridyl)-3-methylbenzenesulfonamide:



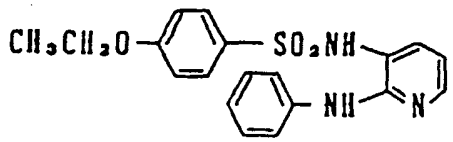
The title compound was produced in the same manner as that of Example 1.

Melting point: 161 to 162°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 340 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 2.22 (3H, s), 6.74 (1H, dd, J=7.6, 4.8Hz), 6.90 (1H, dt, J=7.2, 1.2Hz), 7.21 (2H, t, J=7.2Hz), 7.27-7.35 (3H, m), 7.42 (2H, dd, J=7.2, 1.2Hz), 7.45 (1H, td, J=7.2, 2.0Hz), 7.52 (1H, br-s), 7.92 (1H, s), 8.00 (1H, dd, J=4.8, 1.2Hz), 9.68 (1H, br-s)

Elementary analysis for $C_{18}H_{17}N_3O_2S$:			
	C	H	N
Calculated	63.70	5.05	12.38
Found	63.81	5.16	12.43

Example 27

N-(2-Anilino-3-pyridyl)-4-ethoxybenzenesulfonamide:



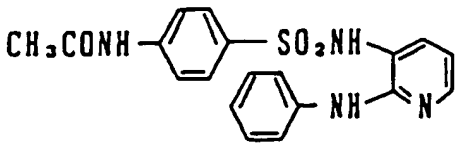
The title compound was produced in the same manner as that of Example 1.

Melting point: 161 to 162°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 370 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 1.26 (3H, t, J=7.0Hz), 3.94 (2H, g, J=7.0Hz), 6.74 (1H, dd, J=7.6, 4.8Hz), 6.89 (1H, tt, J=7.2, 0.8Hz), 6.92 (2H, d, J=8.8Hz), 7.21 (2H, t, J=7.2Hz), 7.27 (1H, dd , J=7.6, 1.6Hz), 7.42 (2H, dd, J=7.2, 0.8Hz), 7.57 (2H, d, J=8.8Hz), 7.88 (1H, s), 7.99 (1H, dd, J=4.8, 1.6Hz), 9.53 (1H, br-s)

Elementary analysis for $C_{19}H_{19}N_3O_3S$:			
	C	H	N
Calculated	61.77	5.18	11.37
Found	61.72	5.31	11.43

Example 28

4-Acetylamino-N-(2-anilino-3-pyridyl)benzenesulfonamide:



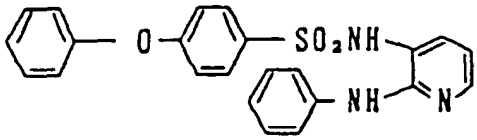
The title compound was produced in the same manner as that of Example 1.

Melting point:	234 to 236°C (recrystallized from methanol)
FAB mass spectrometry m/z:	383 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.04 (3H, s), 6.72 (1H, dd, J=7.6, 4.8Hz), 6.90 (1H, tt, J=8.0, 1.2Hz), 7.19-7.24 (3H, m), 7.45 (2H, dd, J=8.0, 1.2Hz), 7.60 (2H, d, J=9.2Hz), 7.65 (2H, d, J=9.2Hz), 7.91 (1H, s), 7.98 (1H, dd, J=4.8, 1.6Hz), 9.60 (1H, br-s), 10.23 (1H, br-s)

Elementary analysis for $C_{19}H_{18}N_4O_3S$:			
	C	H	N
Calculated	59.67	4.74	14.65
Found	59.69	4.82	14.38

Example 29

N-(2-Anilino-3-pyridyl)-4-phenoxybenzenesulfonamide:



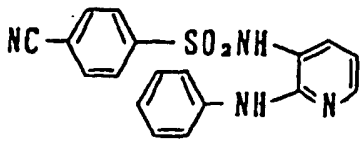
The title compound was produced in the same manner as that of Example 1.

Melting point:	164 to 166°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	418 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	6.78 (1H, dd, J=7.6, 4.8Hz), 6.84 (2H, dd, J=7.6, 1.2Hz), 6.91-6.96 (3H, m), 7.19-7.27 (3H, m), 7.36-7.40 (3H, m), 7.44 (2H, dd, J=7.6, 1.2Hz), 7.62 (2H, d, J=9.2Hz), 7.85 (1H, s), 8.02 (1H, dd, J=4.8, 1.6Hz), 9.62 (1H, br-s)

Elementary analysis for $C_{23}H_{19}N_3O_3S$:			
	C	H	N
Calculated	66.17	4.59	10.06
Found	66.15	4.68	10.04

Example 30

N-(2-Anilino-3-pyridyl)-4-cyanobenzenesulfonamide:



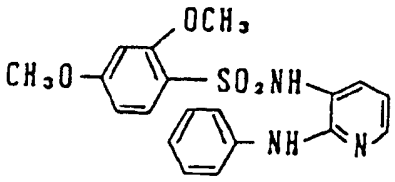
The title compound was produced in the same manner as that of Example 1.

Melting point:	155 to 157°C (recrystallized from methanol)
FAB mass spectrometry m/z:	351 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	6.80 (1H, dd, J=7.6, 4.8Hz), 6.90 (1H, t, J=7.6Hz), 7.20 (2H, t, J=7.6Hz), 7.31 (2H, d, J=7.6Hz), 7.36 (1H, dd, J=7.6, 1.6Hz), 7.76 (2H, d, J=7.6Hz), 7.86-7.89 (3H, m), 8.05 (1H, br), 9.90 (1H, br-s)

Elementary analysis for $C_{18}H_{14}N_4O_2S$:			
	C	H	N
Calculated	61.70	4.03	15.99
Found	61.73	4.14	15.75

Example 31

N-(2-Anilino-3-pyridyl)-2,4-dimethoxybenzenesulfonamide:



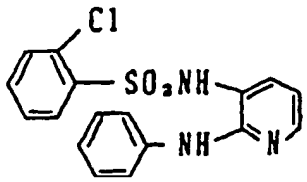
The title compound was produced in the same manner as that of Example 1.

Melting point:	176 to 178°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	386 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.76 (3H, s), 3.81 (3H, s), 6.53 (1H, dd, J=8.8, 2.4Hz), 6.59 (1H, d, J=2.4Hz), 6.69 (1H, dd, J=7.6, 4.8Hz), 6.92 (1H, t, J=7.6Hz), 7.25 (2H, t, J=7.6Hz), 7.33 (1H, dd, J=7.6, 1.6Hz), 7.50 (2H, d, J=7.6Hz), 7.55 (1H, d, J=8.8Hz), 7.92 (1H, dd, J=4.8, 1.6Hz), 8.07 (1H, s)

Elementary analysis for $C_{19}H_{19}N_3O_4S$:			
	C	H	N
Calculated	59.21	4.97	10.90
Found	59.19	5.04	10.91

Example 32

N-(2-Anilino-3-pyridyl)-2-chlorobenzenesulfonamide:



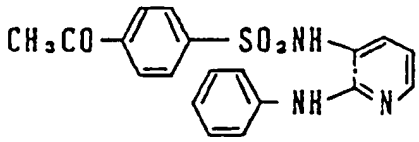
The title compound was produced in the same manner as that of Example 1.

Melting point:	140 to 141°C (recrystallized from toluene)
FAB mass spectrometry m/z:	360 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	6.72 (1H, dd, J=7.6, 4.8Hz), 6.93 (1H, t, J=7.6Hz), 7.25 (2H, t, J=7.6Hz), 7.31 (1H, dd, J=7.6, 1.6Hz), 7.42-7.46 (1H, m), 7.49 (2H, d, J=7.6Hz), 7.56-7.59 (2H, m), 7.87 (1H, d, J=7.6Hz), 7.95-8.01 (2H, m), 10.14 (1H, br-s)

Elementary analysis for $C_{17}H_{14}ClN_3O_2S$:			
	C	H	N
Calculated	56.74	3.92	11.68
Found	56.86	4.06	11.62

Example 33

4-Acetyl-N-(2-anilino-3-pyridyl)benzenesulfonamide:



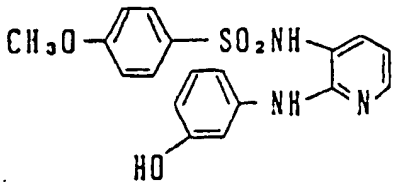
The title compound was produced in the same manner as that of Example 1.

Melting point:	171 to 173°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	368 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.46 (3H, s), 6.78 (1H, dd, J=7.6, 4.8Hz), 6.85 (1H, t, J=7.6Hz), 7.15 (2H, t, J=7.6Hz), 7.31 (2H, dd, J=7.6, 1.2Hz), 7.35 (1H, dd, J=7.6, 1.6Hz), 7.74 (2H, d, J=8.4Hz), 7.85 (1H, s), 7.94 (2H, d, J=8.4Hz), 8.03 (1H, dd, J=4.8, 1.6Hz), 9.83 (1H, br-s)

Elementary analysis for $C_{19}H_{17}N_3O_3S$:			
	C	H	N
Calculated	62.11	4.66	11.44
Found	62.31	4.78	11.19

Example 34

N-[2-[(3-Hydroxyphenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



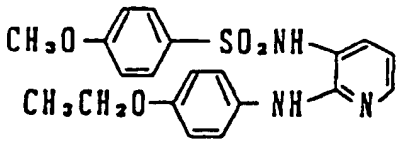
4.0 g (19.9 mmol) of the compound produced in Production Example 6 was reacted with 4.11 g (19.9 mmol) of p-methoxybenzenesulfonyl chloride and the product was treated in the same manner as that of Example 1 to obtain 5.0 g of the title compound.

Melting point: 181 to 182°C (recrystallized from toluene)
FAB mass spectrometry m/z: 372 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.72 (3H, s), 6.31 (1H, dd, J=8.0, 2.0Hz), 6.72 (1H, dd, J=7.6, 4.8Hz), 6.79 (1H, d, J=8.0Hz), 6.96 (2H, d, J=8.8Hz), 6.98 (1H, t, J=8.0Hz), 7.02 (1H, t, J=2.0Hz), 7.25 (1H, dd, J=7.6, 1.6Hz), 7.59 (2H, d, J=8.8Hz), 7.77 (1H, s), 7.99 (1H, dd, J=4.8, 1.6Hz), 9.18 (1H, s), 9.56 (1H, br-s)

Elementary analysis for $C_{18}H_{17}N_3O_4S$:			
	C	H	N
Calculated	58.21	4.61	11.31
Found	58.26	4.67	10.99

Example 35

N-[2-[(4-Ethoxyphenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



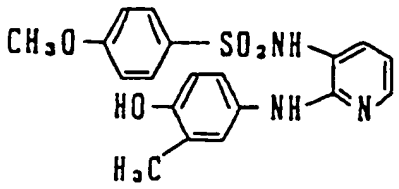
The title compound was produced in the same manner as that of Example 1.

Melting point: 144 to 146°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 400 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 1.31 (3H, t, J=2.8Hz), 3.73 (3H, s), 3.97 (2H, q, J=2.8Hz), 6.65 (1H, dd, J=4.8, 7.6Hz), 6.80 (2H, d, J=8.8Hz), 6.98 (2H, d, J=8.8Hz), 7.21 (1H, dd, J=1.6, 7.6Hz), 7.28 (2H, d, J=8.8Hz), 7.60 (2H, d, J=8.8Hz), 7.72 (1H, br-s), 7.92 (1H, dd, J=1.6, 4.8Hz), 9.47 (1H, br-s)

Elementary analysis for $C_{20}H_{21}N_3O_4S$:			
	C	H	N
Calculated	60.13	5.30	10.52
Found	60.02	5.27	10.21

Example 36

N-[2-[(4-hydroxy-3-methylphenyl) amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



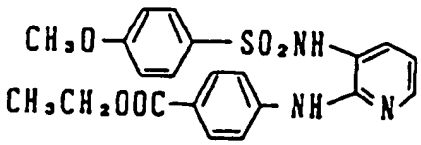
The title compound was produced in the same manner as that of Example 1.

Melting point:	89 to 91°C (recrystallized from toluene)
FAB mass spectrometry m/z:	386 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.07 (3H, s), 3.75 (3H, s), 6.60 (1H, dd, J=4.8, 7.6Hz), 6.63 (1H, d, J=8.4Hz), 6.93 (1H, d, J=2.8Hz), 6.98-7.03 (3H, m), 7.18 (1H, dd, J=1.6, 7.6Hz), 7.50 (1H, br-s), 7.60 (2H, d, J=8.8Hz), 7.88 (1H, dd, J=1.6, 4.8Hz), 8.87 (1H, s), 9.44 (1H, br-s)

Elementary analysis for $C_{19}H_{19}N_3O_4S$:			
	C	H	N
Calculated	59.21	4.97	10.90
Found	58.97	5.06	10.53

Example 37

Ethyl 4-[[3-(4-methoxybenzenesulfonamido)-2-pyridyl]-amino]benzoate:



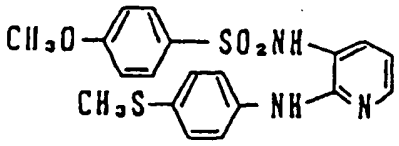
The title compound was produced in the same manner as that of Example 1.

Melting point:	172 to 173°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	428 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	1.31 (3H, t, J=3.2Hz), 3.63 (3H,s), 4.27 (2H, q, J=3.2Hz), 6.88 (2H, d, J=8.8Hz), 6.88 (1H, dd, J=4.8, 7.6Hz), 7.38 (1H, dd, J=1.6, 7.6Hz), 7.51 (2H, d, J=8.8Hz), 7.54 (2H, d, J=8.8Hz), 7.80 (2H, d, J=8.8Hz), 8.10 (1H, dd, J=1.6, 4.8Hz), 8.34 (1H, br-s), 9.58 (1H, br-s)

Elementary analysis for $C_{21}H_{21}N_3O_5S$:			
	C	H	N
Calculated	59.00	4.95	9.83
Found	53.98	4.91	9.63

Example 38

4-Methoxy-N-[2-[(4-methylthiophenyl)amino] -3-pyridyl]-benzenesulfonamide:



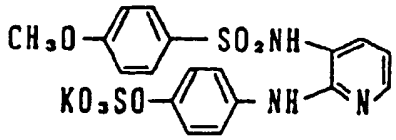
The title compound was produced in the same manner as that of Example 1.

Melting point:	148 to 149°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	402 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.43 (3H, s), 3.70 (3H, s), 6.73 (1H, dd, J=4.8, 7.6Hz), 6.94 (2H, d, J=8.8Hz), 7.17 (2H, d, J=8.8Hz), 7.26 (1H, dd, J=1.6, 7.6Hz), 7.39 (2H, d, J=8.8Hz), 7.57 (2H, d, J=8.8Hz), 7.93 (1H, br-s), 7.98 (1H, dd, J=1.6, 4.8Hz), 9.51 (1H, br-s)

Elementary analysis for $C_{19}H_{19}N_3O_3S_2$:			
	C	H	N
Calculated	56.84	4.77	10.47
Found	56.90	4.77	10.24

Example 39

Potassium 4-[[3-(4-methoxybenzenesulfonamido)-2-pyridyl]amino]phenyl sulfate:



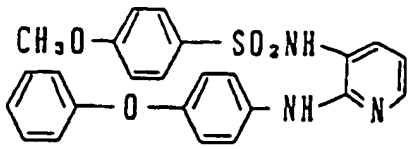
2.0 g (5.38 mmol) of the compound of Example 6 was dissolved in 20 ml of pyridine. 800 mg (6.87 mmol) of chlorosulfonic acid (95%) was added dropwise thereto at -15 to -10°C. The temperature was slowly elevated to room temperature and the mixture was stirred for 3 days. A 1 N aqueous potassium carbonate solution was added to the reaction mixture to adjust the pH to 8 to 9. The solvent was distilled off under reduced pressure. Water and ethyl acetate were added to the residue and an aqueous layer thus formed was separated, concentrated, purified by silica gel column chromatography and precipitated with methanol/dichloromethane to obtain 1.58 g of the title compound.

Melting point:	165 to 166°C
FAB mass spectrometry m/z:	528 ($[M+K]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.73 (3H, s), 6.68 (1H, dd, J=4.8, 8.0Hz), 6.98 (2H, d, J=8.8Hz), 7.02 (2H, d, J=8.4Hz), 7.25-7.27 (3H, m), 7.61 (2H, d, J=8.8Hz), 7.83 (1H, s), 7.94 (1H, dd, J=1.2, 4.8Hz), 9.55 (1H, s)

Elementary analysis for $C_{18}H_{16}N_3O_7S_2K \cdot 3/2H_2O$:			
	C	H	N
Calculated	41.85	3.71	8.13
Found	41.88	3.41	8.08

Example 40

4-Methoxy-N-[2-[(4-phenoxyphenyl)amino]-3-pyridyl]benzenesulfonamide:



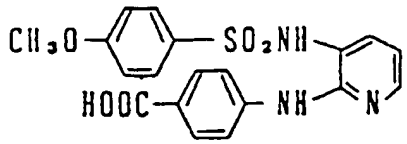
The title compound was produced in the same manner as that of Example 1.

Melting point:	174 to 176°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	448 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.75 (3H, s), 6.72 (1H, dd, J=4.8, 7.6Hz), 6.92 (2H, d, J=8.8Hz), 6.91-6.97 (2H, m), 6.96 (2H, d, J=8.8Hz), 7.05-7.10 (1H, m), 7.27 (1H, dd, J=1.6, 7.6Hz), 7.32-7.40 (2H, m), 7.43 (2H, d, J=8.8Hz), 7.59 (2H, d, J=8.8Hz), 7.92 (1H, br-s), 7.98 (1H, dd, J=1.6, 4.8Hz), 9.44 (1H, br-s)

Elementary analysis for $C_{24}H_{21}N_3O_4S$:			
	C	H	N
Calculated	64.41	4.73	9.39
Found	64.71	4.96	9.30

Example 41

4-[[3-(4-Methoxybenzenesulfonamido)-2-pyridyl]amino]benzoic acid:



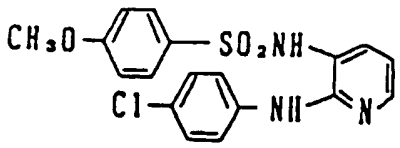
The title compound was produced by an alkaline hydrolysis of the compound of Example 37 in an ordinary manner.

Melting point:	248 to 250°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	400 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.64 (3H, s), 6.87 (1H, dd, J=4.8, 7.6Hz), 6.89 (2H, d, J=8.8Hz), 7.37 (1H, dd, J=1.6, 7.6Hz), 7.49 (2H, d, J=8.8Hz), 7.54 (2H, d, J=8.8Hz), 7.78 (2H, d, J=8.8HZ), 8.09 (1H, dd, J=1.6, 4.8Hz), 8.29 (1H, br-s), 9.58 (1H, br-s), 12.44 (1H, br)

Elementary analysis for $C_{19}H_{17}N_3O_5S$:			
	C	H	N
Calculated	57.13	4.29	10.52
Found	57.10	4.42	10.35

Example 42

N-[2-[(4-Chlorophenyl)amino]-3-pyridyl] -4-methoxybenzenesulfonamide:



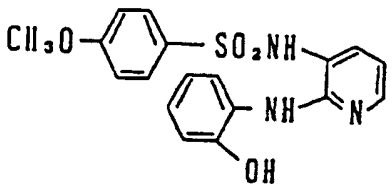
The title compound was produced in the same manner as that of Example 1.

Melting point: 205 to 207°C (decomp.) (recrystallized from ethanol)
FAB mass spectrometry m/z: 390 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.70 (3H, s), 6.78 (1H, dd, J=7.6, 4.8Hz), 6.93 (2H, d, J=8.8Hz), 7.24 (2H, d, J=8.8Hz), 7.30 (1H, dd, J=7.6, 2.0Hz), 7.45 (2H, d, J=8.8Hz), 7.56 (2H, d, J=8.8Hz), 8.02 (1H, dd, J=4.8, 2.0Hz), 8.05 (1H, s), 9.51 (1H, br-s)

Elementary analysis for $C_{18}H_{16}ClN_3O_3S$:			
	C	H	N
Calculated	55.46	4.14	10.78
Found	55.44	4.32	10.71

Example 43

N-[2-[(2-Hydroxyphenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



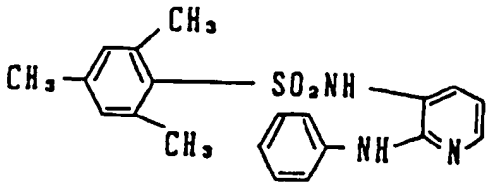
The title compound was produced in the same manner as that of Example 1.

Melting point: 154 to 155°C (recrystallized from toluene)
FAB mass spectrometry m/z: 372 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.81 (3H, s), 6.63 (1H, dd, J=8.0, 5.2Hz), 6.72-6.79 (2H, m), 6.82-6.86 (2H, m), 7.07 (2H, d, J=8.8Hz), 7.66 (2H, d, J=8.8Hz), 8.05 (1H, dd, J=5.2, 1.6Hz), 8.15 (1H, s), 8.29 (1H, dd, J=7.6, 2.0Hz), 9.70 (1H, s), 9.94 (1H, s)

Elementary analysis for $C_{18}H_{17}N_3O_4S$:			
	C	H	N
Calculated	58.22	4.61	11.32
Found	58.39	4.60	11.20

Example 44

N-(2-Anilino-3-pyridyl) -2,4,6-trimethylbenzenesulfonamide:



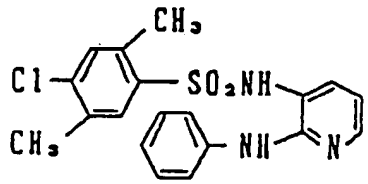
The title compound was produced in the same manner as that of Example 1.

Melting point:	140 to 142°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	368 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.16 (3H, s), 2.41 (6H, s), 6.70 (1H, dd, J=7.6, 4.8Hz), 6.89-6.94 (3H, m), 7.08 (1H, dd, J=7.6, 1.6Hz), 7.24 (2H, t, J=7.6Hz), 7.43 (2H, d, J=7.6Hz), 7.89 (1H, s), 8.01 (1H, dd, J=4.8, 1.6Hz), 9.58 (1H, s)

Elementary analysis for $C_{20}H_{21}N_3O_2S$:			
	C	H	N
Calculated	65.37	5.76	11.43
Found	65.45	5.67	11.34

Example 45

N-(2-Anilino-3-pyridyl)-4-chloro-2,5-dimethylbenzenesulfonamide:



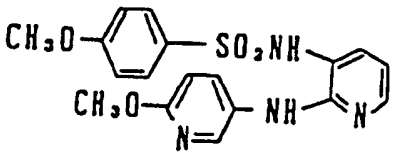
The title compound was produced in the same manner as that of Example 1.

Melting point:	153 to 154°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	388 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.20 (3H, s), 2.41 (3H, s), 6.75 (1H, dd, J=7.6, 4.8Hz), 6.91 (1H, t, J=7.6Hz), 7.23 (2H, t, J=7.6Hz), 7.26 (1H, dd, J=7.6, 1.6Hz), 7.33 (1H, s), 7.38 (2H, d, J=7.6Hz), 7.63 (1H, s), 7.93 (1H, s), 8.02 (1H, dd, J=4.8, 1.6Hz), 9.76 (1H, s)

Elementary analysis for $C_{19}H_{18}ClN_3O_2S$:			
	C	H	N
Calculated	58.83	4.68	10.83
Found	58.97	4.64	10.85

Example 46

4-Methoxy-N-[2-[(2-methoxy-5-pyridyl)amino]-3-pyridyl]benzenesulfonamide:



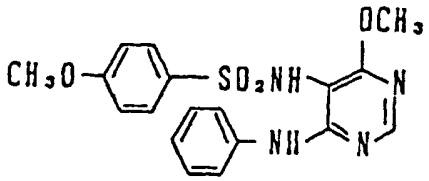
The title compound was produced in the same manner as that of Example 1.

Melting point:	159 to 160°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	387 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.73 (3H, s), 3.81 (3H, s), 6.68-6.73 (2H, m), 6.98 (2H, d, J=8.8Hz), 7.25 (1H, dd, J=7.6, 1.2Hz), 7.60 (2H, d, J=8.8Hz), 7.72 (1H, dd, J=8.8, 2.8Hz), 7.90 (1H, s), 7.93 (lH, dd, J=4.8, 1.2Hz), 8.13 (1H, d, J=2.8Hz), 9.44 (lH, br-s)

Elementary analysis for $C_{18}H_{18}N_4O_4S$:			
	C	H	N
Calculated	55.95	4.69	14.50
Found	55.95	4.72	14.46

Example 47

N- (4-Anilino-6-methoxy-5-pyrimidyl) -4-methoxybenzenesulfonamide:



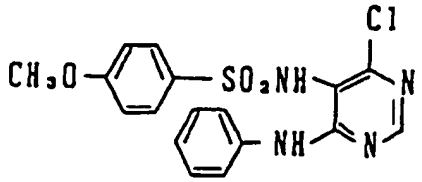
The title compound was produced in the same manner as that of Example 1.

Melting point:	159 to 160°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	387 ([M+H$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.38 (3H, s), 3.80 (3H, s), 7.01-7.07 (3H, m), 7.30 (2H, t, J=8.0Hz), 7.57 (2H, dd, J=8.0, 0.8Hz), 7.63 (2H, d, J=8.8Hz), 8.20 (1H, s), 8.33 (1H, s), 9.29 (1H, s)

Elementary analysis for $C_{18}H_{18}N_4O_4S$:			
	C	H	N
Calculated	55.95	4.70	14.50
Found	55.90	4.71	14.49

Example 48

N-(4-Anilino-6-chloro-5-pyrimidyl)-4-methoxybenzenesulfonamide:



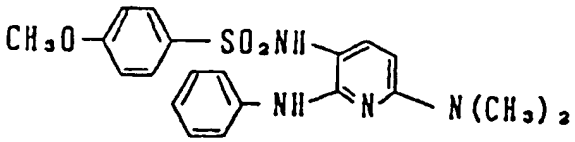
The title compound was produced in the same manner as that of Example 1.

Melting point: 174 to 175°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 391 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.75 (3H, s), 7.03 (2H, d, J=8.8Hz), 7.09 (1H, t, J=7.6Hz), 7.32 (2H, t, J=7.6Hz), 7.46 (2H, d, J=7.6Hz), 7.65 (2H, d, J=8.8Hz), 8.29 (1H, s), 8.63 (1H, s), 9.74 (1H, br-s)

Elementary analysis for $C_{17}H_{15}N_4O_3SCl$:			
	C	H	N
Calculated	52.24	3.87	14.33
Found	52.29	3.85	14.27

Example 49

N-(2-Anilino-6-dimethylamino-3-pyridyl)-4-methoxybenzenesulfonamide:



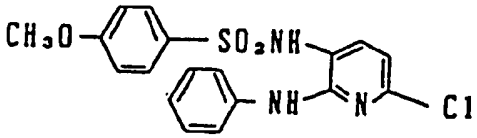
The title compound was produced in the same manner as that of Example 1.

Melting point: 152 to 153°C (recrystallized from ethyl acetate/ n-hexane):
FAB mass spectrometry m/z: 399 ([M+H]$^+$)
^{1}H-NMR ($CDCl_3$) δ (ppm): 3.04 (6H, s), 3.83 (3H, s), 5.71 (1H, d, J=8.8Hz), 5.75 (1H, s), 6.59 (1H, d, J=8.8Hz), 6.91-6.96 (3H, m), 7.24-7.28 (3H, m), 7.53 (2H, d, J=7.6Hz), 7.72 (2H, d, J=9.2Hz)

Elementary analysis for $C_{20}H_{22}N_4O_3S$:			
	C	H	N
Calculated	60.28	5.56	14.06
Found	60.21	5.47	13.92

Example 50

N-(2-Anilino-6-chloro-3-pyridyl)-4-methoxybenzenesulfonamide:



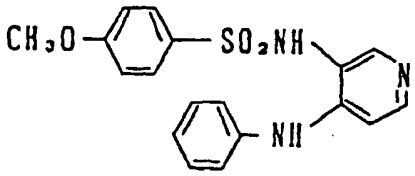
The title compound was produced in the same manner as that of Example 1.

Melting point:	206 to 208°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	390 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.71 (3H, s), 6.79 (1H, d, J=8.0Hz), 6.93-6.99 (3H, m), 7.26 (3H, t, J=8.0Hz), 7.38 (2H, d, J=8.0Hz), 7.61 (2H, d, J=9.2Hz), 8.15 (1H, s), 9.56 (1H, s)

Elementary analysis for $C_{18}H_{16}ClN_3O_3S$:			
	C	H	N
Calculated	55.46	4.14	10.78
Found	55.49	4.04	10.62

Example 51

N-(4-Anilino-3-pyridyl)-4-methoxybenzenesulfonamide:



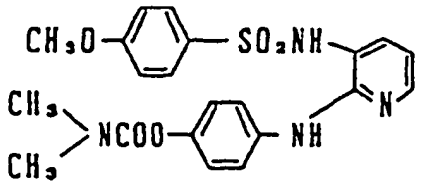
The title compound was produced in the same manner as that of Example 1.

Melting point:	201 to 202°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	356 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ(ppm):	3.75 (3H, s), 6.92 (1H, d, J=6.4Hz), 6.95 (2H, d, J=8.8Hz), 7.13-7.20 (3H, m), 7.39 (2H, t, J=8.0Hz), 7.67 (2H, d, J=8.8Hz), 7.78 (1H, s), 7.82 (1H, d, J=5.6Hz)

Elementary analysis for $C_{18}H_{17}N_3O_3S$:			
	C	H	N
Calculated	60.83	4.82	11.82
Found	60.78	4.77	11.84

Example 52

N- [2-[(4-Dimethylcarbamoyloxyphenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



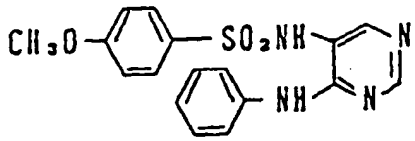
The title compound was produced in the same manner as that of Example 1.

Melting point:	202 to 203°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	443 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.90 (3H, s), 3.03 (3H, s), 3.72 (3H, s), 6.72 (1H, dd, J=7.6, 4.8Hz), 6.96 (2H, d, J=8.8Hz), 6.97 (2H, d, J=8.8Hz), 7.26 (1H, dd, J=7.6, 1.6Hz), 7.41 (2H, d, J=8.8Hz), 7.60 (2H, d, J=8.8Hz), 7.94 (1H, s), 7.97 (1H, dd, J=4.8, 1.6Hz), 9.52 (1H, br-s)

Elementary analysis for $C_{21}H_{22}N_4O_5S$:			
	C	H	N
Calculated:	57.00	5.01	12.66
Found:	57.35	4.98	12.55

Example 53

N-(4-Anilino-5-pyrimidyl)-4-methoxybenzenesulfonamide:



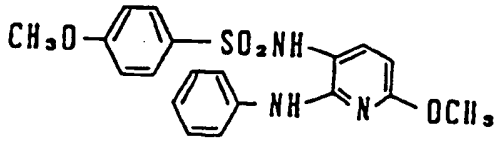
The title compound was produced by catalytically reducing the compound of Example 48 in the presence of palladium/carbon in an ordinary manner.

Melting point:	189 to 190°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	357 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.73 (3H, s), 7.01 (2H, d, J=8.8Hz), 7.05 (1H, t, J=8.0Hz), 7. 30 (2H, t, J=8.0Hz), 7.50 (2H, d, J=8.0Hz), 7.64 (2H, d, J=8.8Hz), 7.87 (1H, s), 8.40 (1H, s), 8.57 (1H, br-s)

Elementary analysis for $C_{17}H_{16}N_4O_3S$:			
	C	H	N
Calculated	57.29	4.53	15.72
Found	57.25	4.68	15.36

Example 54

N-(2-Anilino-6-methoxy-3-pyridyl)-4-methoxybenzenesulfonamide:



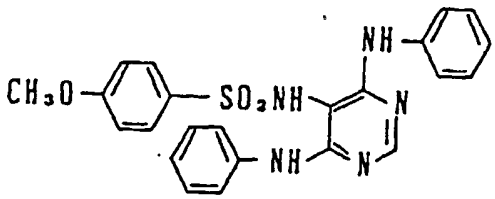
The title compound was produced in the same manner as that of Example 1.

Melting point:	187 to 188°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	386 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.70 (3H, s), 3.77 (3H, s), 6.11 (1H, d, J=8.0Hz), 6.89 (1H, t, J=7.6Hz), 6.95 (2 H, d, J=9.2Hz), 7.07 (1H, d, J=8.0Hz), 7.22 (2H, t, J=7.6Hz), 7.43 (2H, d, J=7.6Hz), 7.52 (2H, d, J=9.2Hz), 7.83 (1H, br-s), 9.23 (1H, br-s)

Elementary analysis for $C_{19}H_{19}N_3O_4S$:			
	C	H	N
Calculated	59.21	4.97	10.90
Found	59.32	4.97	10.76

Example 55

N-(4,6-Dianilino-5-pyrimidyl)-4-methoxybenzenesulfonamide:



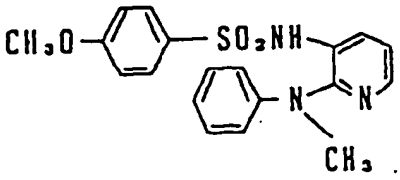
The title compound was produced in the same manner as that of Example 1.

Melting point:	149 to 151°C (recrystallized from dichloromethane/n-hexane)
FAB mass spectrometry m/z:	448 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.53 (3H, s), 6.82 (2H, d, J=8.8Hz), 6.96 (2H, t, J=7.6Hz), 7.23 (4H, t, J=7.6Hz), 7.40 (4H, d, J=7.6Hz), 7.62 (2H, d, J=8.8Hz), 8.05 (2H, s), 8.11 (1H, s), 8.90 (1H, s)

Elementary analysis for $C_{23}H_{21}N_5O_3S$:			
	C	H	N
Calculated	61.73	4.73	15.65
Found	61.91	4.72	15.74

Example 56

4-Methoxy-N-(2-(methylphenyl)amino-3-pyridyl]benzenesulfonamide:



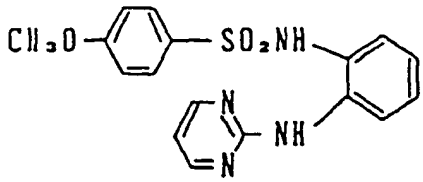
The title compound was produced in the same manner as that of Example 1.

Melting point: 80 to 81°C (recrystallized from diisopropyl ether)
FAB mass spectrometry m/z: 370 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.01 (3H, s), 3.82 (3H, s), 6.46-6.51 (2H, m), 6.78-6.84 (1H, m), 7.04 (2H, d, J=8.8Hz), 7.11-7.17 (2H, m), 7.17 (1H, dd, J=4.8, 8.0Hz), 7.65 (1H, dd, J=1.6, 8.0Hz), 7.68 (2H, d, J=8.8Hz), 8.14 (1H, dd, J=1.6, 4.8Hz), 9.30 (1H, br-s)

Elementary analysis for $C_{19}H_{19}N_3O_3S$:			
	C	H	N
Calculated	61.77	5.18	11.38
Found	61.85	5.28	11.36

Example 57

4-Methoxy-N-[2-[(2-pyrimidyl)amino]phenyl]benzenesulfonamide:



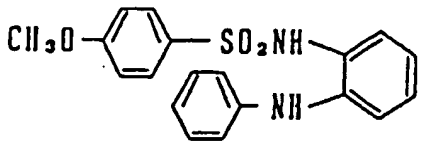
The title compound was produced in the same manner as that of Example 1.

Melting point: 193 to 195°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 357 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.70 (3H, s), 6.79-6.83 (3H, m), 6.96 (1H, dt, J=1.6, 8.4Hz), 7.01 (1H, dd, J=1.6, 8.4Hz), 7.19 (1H, dt, J=1.6, 8.4Hz), 7.47 (2H, d, J=8.8Hz), 7.87 (1H, dd, J=1.6, 8.4Hz), 8.38 (2H, dd, J=1.6, 4.8Hz), 8.54 (1H, br-s), 9.53 (1H, br-s)

Elementary analysis for $C_{17}H_{16}N_4O_3S$:			
	C	H	N
Calculated	57.29	4.53	15.72
Found	57.18	4.57	15.80

Example 58

N-(2-Anilinophenyl)-4-methoxybenzenesulfonamide:



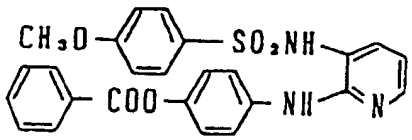
The title compound was produced in the same manner as that of Example 1.

Melting point:	140 to 142°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	354 (M^+)
^{1}H-NMR (DMSO-d_6) δ (ppm):	3.69 (3H, s), 6.66-6.72 (2H, m), 6.81 (2H, d, J=8.8Hz), 6.76-6.87 (2H, m), 7.04-7.17 (5H, m), 7.24 (1H, br-s), 7.52 (2H, d, J=8.8Hz), 9.30 (1H, br-s)

Elementary analysis for $C_{19}H_{18}N_2O_3S$:			
	C	H	N
Calculated	64.39	5.12	7.90
Found	64.49	5.17	7.77

Example 59

N-[2-[(4-Benzoyloxyphenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



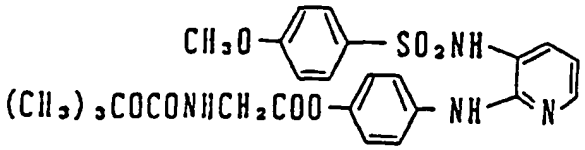
The title compound was produced in the same manner as that of Example 1.

Melting point:	208 to 210°C (recrystallized from methanol)
FAB mass spectrometry m/z:	476 ($[M+H]^+$)
1H-NMR (DMSO-d_6) δ (ppm):	3.73 (3H, s), 6.75 (1H, d, J=4.8, 7.6Hz), 6.98 (2H, d, J=8.8Hz), 7.13 (2H, d, J=8.8Hz), 7.28 (1H, dd, J=1.6, 7.6Hz), 7.51 (2H, d, J=8.8Hz), 7.61 (2H, d, J=8.8Hz), 7.58-7.65 (2H, m), 7.72-7.78 (1H, m), 8.00 (1H, dd, J=1.6, 4.8Hz), 8.04 (1H, br-s), 8.11-8.16 (2H,m), 9.54 (1H, br-s)

Elementary analysis for $C_{25}H_{21}N_3O_5S$:			
	C	H	N
Calculated	63.15	4.45	8.84
Found	62.95	4.57	8.76

Example 60

N-[2-[[4-(tert-Butoxycarbonylaminoacetyloxy)phenyl]amino]-3-pyridyl]-4-methoxybenzenesulfonamide:

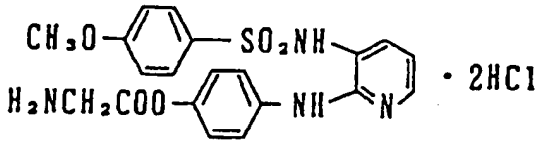


The title compound was produced in the same manner as that of Example 1.

^{1}H-NMR ($CDCl_3$) δ (ppm): 1.47 (9H, s), 3.82 (3H, s), 4.18 (2H, d, J=5.6Hz), 5.17 (1H, br-s), 6.58 (2H, dd, J=7.6, 4.8Hz), 6.89 (1H, dd, J=7.6, 1.6Hz), 6.90 (2H, d, J=8.8Hz), 7.00 (2H, d, J=8.8Hz), 7.35 (1H, br-s), 7.47 (2H, d, J=8.8Hz), 7.68 (2H, d, J=8.8Hz), 8.10 (1H, dd, J=4.8, 1.6Hz)

Example 61

N-[2-[[4-(Aminoacetyloxy)phenyl]amino]-3-pyridyl]-4-methoxybenzenesulfonamide dihydrochloride:



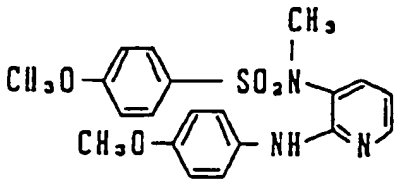
272 mg (0.515 mmol) of the compound of Example 60 was added to 10 ml of tetrahydrofuran. 2 ml of concentrated hydrochloric acid was added to the mixture and stirred at room temperature for 3 h. The solvent was distilled off under reduced pressure and the residue was recrystallized from ethanol to obtain 159 mg of the title compound.

Melting point: 196 to 199°C (decomp.)
FAB mass spectrometry m/z: 429 ($(M+H)^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.71 (3H, s), 4.08-4.11 (2H, m), 6.78 (1H, dd, J=4.8, 7.6Hz), 6.94 (2H, d, J=8.8Hz), 7.04 (2H, d, J=8.8Hz), 7.32 (1H, dd, J=1.6, 7.6Hz), 7.48-7.51 (2H, m), 7.61 (2H, d, J=8.8Hz), 7.97 (1H, dd, J=1.6, 4.8Hz), 8.48 (3H, br-s), 9.84 (1H, br-s)

Elementary analysis for $C_{20}H_{20}N_4O_5S \cdot 2HCl \cdot 1/2H_2O$:			
	C	H	N
Calculated	47.07	4.54	10.98
Found	47.38	4.45	10.78

Example 62

4-Methoxy-N-[2-[(4-methoxyphenyl)amino]-3-pyridyl]-N-methylbenzenesulfonamide:



500 mg (1.3 mmol) of the compound of Example 4 was dissolved in 5 ml of dimethylformamide. 60 mg (1.5 mmol) of sodium hydride (60%) was added to the solution. The resulting solution was stirred at room temperature for 30 min and 95 µl (1.5 mmol) of methyl iodide was added thereto.

After stirring overnight, the solvent was distilled off under reduced pressure. The resultant residue was dissolved in ethyl acetate and the solution was washed with water. After drying over magnesium sulfate, it was concentrated and purified by silica gel column chromatography to obtain 290 mg of the title compound.

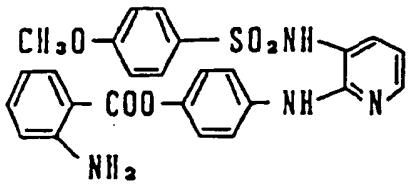
FAB mass spectrometry m/z: 400 ([M+H]$^+$)

^{1}H-NMR ($CDCl_3$) δ (ppm): 3.15 (3H, s), 3.80 (3H, s), 3. 88 (3H, s), 6.50 (1H, dd, J=4.8, 7.6Hz), 6.67 (1H, dd, J=1.6, 7.6Hz), 6.89 (2H, d, J=8.8Hz), 6.98 (2H, d, J=8.8Hz), 7.29 (1H, br-s), 7.47 (2H, d, J=8.8Hz), 7.65 (2H, d, J=8.8Hz), 8.09 (1H, dd, J=1.6, 4.8Hz)

Elementary analysis for $C_{20}H_{21}N_3O_4S$:			
	C	H	N
Calculated	60.14	5.30	10.52
Found	60.08	5.39	10.29

Example 63

N-[2-[[4-(2-Aminobenzoyloxy)phenyl]amino]-3-pyridyl]-4-methoxybenzenesulfonamide:



500 mg (1.35 mmol) of the compound of Example 6, 260 mg (1.59 mmol) of isatoic anhydride and 170 mg (1.39 mmol) of 4-dimethylaminopyridine were dissolved in 5 ml of dimethylformamide and the solution was stirred at 80°C for 5 h. The solvent was distilled off under reduced pressure and ethyl acetate was added to the residue. A precipitate thus formed was recrystallized from ethanol to obtain 500 mg of the title compound.

Melting point: 221 to 225°C (decomp.)

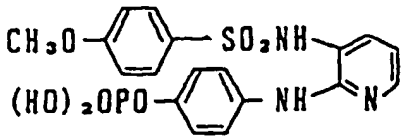
FAB mass spectrometry m/z: 491 ([M+H]$^+$)

^{1}H-NMR (DMSO-d_6) δ (ppm): 3.74 (3H, s), 6.60 (1H, td, J=1.6, 8.4Hz), 6.73 (2H, br-s), 6.74 (1H, dd, J=4.8, 8.0Hz), 6.83 (1H, dd, J=0.8, 8.4Hz), 6.98 (2H, d, J=8.8Hz), 7.08 (2H, d, J=9.2Hz), 7.27 (1H, dd, J=2.0, 8.0Hz), 7.33 (1H, td, J=1.6, 7.2Hz), 7.49 (1H, d, J=9.2Hz), 7.61 (2H, d, J=8.8Hz), 7.92 (1H, dd, J=1.6, 8.4Hz), 7.99 (1H, dd, J=2.0, 4.8Hz), 8.02 (1H, s), 9.60 (1H, br-s)

Elementary analysis for $C_{25}H_{22}N_4O_5S$:			
	C	H	N
Calculated:	61.21	4.52	11.42
Found:	60.98	4.52	11.24

Example 64

4-[[3-(4-Methoxybenzenesulfonamido)-2-pyridyl]amino]phenyl dihydrogenphosphate:



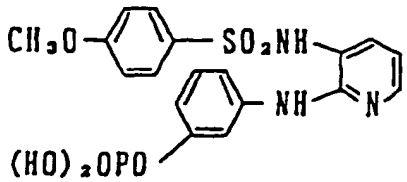
7.44 g (20 mmol) of the compound of Example 6 was suspended in 100 ml of phosphorus oxychloride and the suspension was heated under reflux until a homogeneous solution was obtained. Phosphorus oxychloride was distilled off under reduced pressure and then diisopropyl ether was added to the residue to form a solid, which was separated by filtration and suspended in 100 ml of tetrahydrofuran. 50 ml of water was added to the suspension under cooling with ice and stirred until a homogeneous solution was obtained. After the solvent was distilled off under reduced pressure, 100 ml of methanol and 100 ml of water were added to the residue to obtain a solution, which was concentrated under reduced pressure until an insoluble matter was formed. The insoluble matter was removed and the residue was further concentrated under reduced pressure and the resultant precipitate was separated by filtration to obtain 4.27 g of the title compound.

Melting point: 215 to 216°C
FAB mass spectrometry m/z: 452 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.73 (3H, s), 6.70 (1H, dd, J=7.6, 4.8Hz), 6.98 (2H, d, J=8.8Hz), 7.02 (2H, d, J=8.8Hz), 7.24 (1H, dd, J=7.6, 1.6Hz), 7.35 (2H, d, J=8.8Hz), 7.60 (2H, d, J=8.8Hz), 7.88 (1H, s), 7.95 (1H, dd, J=4.8, 1.6Hz), 9.50 (1H, br-s)

Elementary analysis for $C_{18}H_{18}N_3O_7PS$:			
	C	H	N
Calculated	47.90	4.02	9.31
Found	47.72	4.00	9.39

Example 65

3-[[3-(4-Methoxybenzenesulfonamido)-2-pyridyl]amino]-phenyl dihydrogenphosphate:



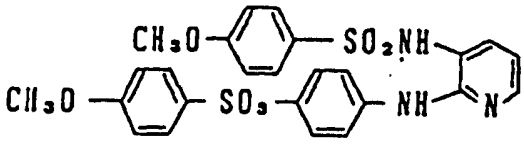
120 mg of the title compound was produced by reacting 1.00 g (2.7 mmol) of the compound of Example 34 with 10 ml of phosphorus oxychloride and the product was treated in the same manner as that of Example 64.

Melting point: 166 to 168°C
FAB mass spectrometry m/z: 452 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ(ppm): 3.70 (3H, s), 6.73 (1H, d, J=7.6Hz), 6.77 (1H, dd, J=7.6, 4.8Hz), 6.95 (2H, d, J=8.8Hz), 7.15 (1H, t, J=7.6Hz), 7.21 (1H, d, J=7.6Hz), 7.30 (1H, dd, J=7.6, 1.6Hz), 7.37 (1H, s), 7.59 (2H, d, J=8.8Hz), 8.01 (1H, dd, J=4.8, 1.6Hz), 8.10 (1H, s), 9.61 (1H, br-s)

Elementary analysis for $C_{18}H_{18}N_3O_7PS \cdot H_2O$:			
	C	H	N
Calculated	46.06	4.29	8.95
Found	46.16	4.13	8.83

Example 66

4-Methoxy-N- [2-[[4- (4-methoxybenzenesulfonyloxy)-phenyl]amino] -3-pyridyl]benzenesulfonamide:



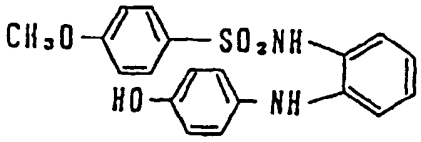
The compound produced in Production Example 4 was reacted with 4-methoxybenzenesulfonyl chloride in an equivalent ratio of 1:2 to obtain the title compound.

Melting point: 122 to 123°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 542 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.71 (3H, s), 3.88 (3H, s), 6.76 (1H, dd, 3=7.6, 4.8Hz), 6.84 (2H, d, J=8.8Hz), 6.94 (2H, d, J=8.8Hz), 7.17 (2H, d, J=8.8Hz), 7.25 (1H, dd, J=7.6, 1.2Hz), 7.42 (2H, d, J=8.8Hz), 7.56 (2H, d, J=8.8Hz), 7.76 (2H, d, J=8.8Hz), 7.98 (1H, dd, J=4.8, 1.2Hz), 8.06 (1H, s), 9.51 (1H, br-s)

Elementary analysis for $C_{25}H_{23}N_3O_7S_2$:			
	C	H	N
Calculated	55.40	4.28	7.76
Found	55.57	4.26	7.61

Example 67

N-[2-[(4-Hydroxyphenyl)amino]phenyl]-4-methoxybenzenesulfonamide:



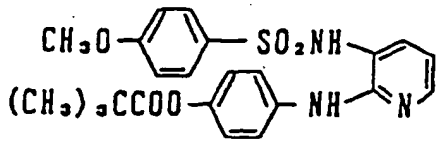
The title compound was produced in the same manner as that of Example 1.

Melting point: 163 to 164°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 370 (M+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.76 (3H, s), 6.58-6.67 (5H, m), 6.77 (1H, br-s), 6.80 (1H, dd, J=1.6, 8.0Hz), 6.90-7.00 (4H, m), 7.56 (2H, d, J=8.8Hz), 9.05 (1H, s), 9.23 (1H, br-s)

Elementary analysis for $C_{19}H_{18}N_2O_4S$:			
	C	H	N
Calculated	61.61	4.90	7.56
Found	61.86	4.90	7.39

Example 68

4-Methoxy-N-[2-[(4-pivaloyloxyphenyl)amino]-3-pyridyl]benzenesulfonamide:



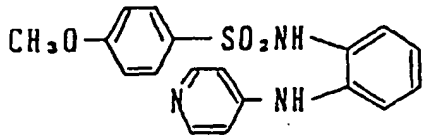
The title compound was produced in the same manner as that of Example 1.

Melting point: 188 to 189°C (recrystallized from toluene)
FAB mass spectrometry m/z: 456 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 1.30 (9H, s), 3.72 (3H, s), 6.73 (1H, dd, J=7.6, 4.8Hz), 6.94 (2H, d, J=8.8Hz), 6.97 (2H, d, J=8.8Hz), 7.25 (1H, dd, J=7.6, 1.6Hz), 7.45 (2H, d, J=8.8Hz), 7.60 (2H, d, J=8.8Hz), 7.97-8.00 (2H, m), 9.52 (1H, br-s)

Elementary analysis for $C_{23}H_{25}N_3O_5S$:			
	C	H	N
Calculated	60.64	5.53	9.22
Found	60.57	5.43	8.95

Example 69

4-Methoxy-N-[2-[(4-pyridyl)amino]phenyl]benzenesulfonamide:



The title compound was produced in the same manner as that of Example 1.

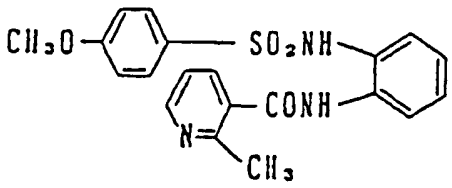
Melting point: 185 to 187°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 356 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.67 (3H, s), 6.45 (2H, d, J=6.0Hz), 6.73 (2H, d, J=8.8Hz), 7.07 (1H, dt, J=7.6, 1.2Hz), 7.16 (1H, dt, J=7.6, 1.2Hz), 7.22 (1H, dd, J=7.6, 1.2Hz), 7.28 (1H, dd, J=7.6, 1.2Hz), 7.45 (2H, d, J=8.8Hz), 7.90 (1H, br-s), 8.05 (2H, d,

J=6.0Hz)

Elementary analysis for $C_{18}H_{17}N_3O_3S$:			
	C	H	N
Calculated	60.83	4.82	11.82
Found	61.08	4.86	11.87

Example 70

N-[2-(4-Methoxybenzenesulfonamido)phenyl]-2-methylnicotinamide:



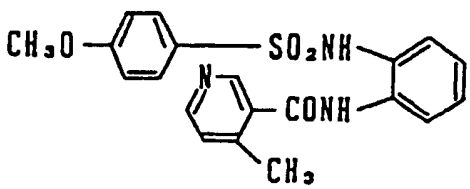
0.97 g (7 mmol) of 2-methylnicotinic acid was suspended in 4.5 ml of dichloromethane. 1.33 g (16.8 mmol) of pyridine and then 1.05 g (8.4 mmol) of thionyl chloride were added to the solution. The mixture was stirred at room temperature for 30 min and then a solution of 1.77 g (6.36 mmol) of the compound produced in Production Example 12 in 7 ml of dichloromethane was added thereto. After stirring overnight, an aqueous sodium hydrogencarbonate solution was added thereto and the product was extracted with dichloromethane. After concentration, ethanol was added to the concentrate and crystals thus formed were separated by filtration and recrystallized from ethanol to obtain 0.80 g of the title compound.

Melting point:	148 to 149°C
FAB mass spectrometry m/z:	398 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.56 (3H, s), 3.80 (3H, s), 7.02 (2H, d, J=8.8Hz), 7.08 (1H, dd, J=2.0, 8.4Hz), 7.11 (1H, dt, J=1.6, 4.4Hz), 7.18-7.27 (1H, m), 7.37 (1H, dd, J=4.8, 7.6Hz), 7.57 (2H, d, J=8.8Hz), 7.71-7.84 (2H, m), 8.58 (1H, dd, J=1.6, 4.8Hz), 9.37 (1H, br-s), 9.60 (1H, br-s)

Elementary analysis for $C_{20}H_{19}N_3O_4S$:			
	C	H	N
Calculated	60.44	4.82	10.57
Found	60.37	4.90	10.41

Example 71

N-[2-(4-Methoxybenzenesulfonamido)phenyl]-4-methylnicotinamide:

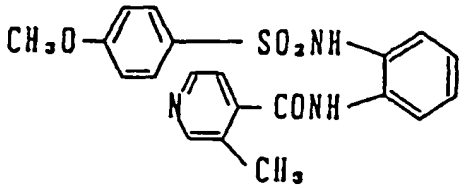


The title compound was produced in the same manner as that of Example 70.

Melting point:	199 to 200°C (recrystallized from methanol)
FAB mass spectrometry m/z:	398 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.58 (39, s), 3.81 (3H, s), 7.00-7.07 (3H, m), 7.09-7. 18 (IH, m), 7.19-7.27 (1H, m), 7.62 (2H, d, J=8.4Hz), 7.74-7.80 (IH, m), 7.82 (1H, d, J=5.6Hz), 8.80 (1H, d, J=5.6Hz), 8.87 (1H, s), 9.62 (1H, br-s), 10.16 (1H, br-s)

Example 72

N- [2-(4-Methoxybenzenesulfonamido)phenyl]-3-methylisonicotinamide:



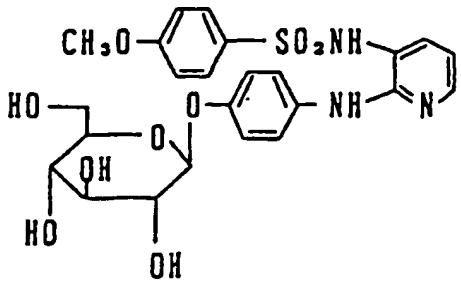
The title compound was produced in the same manner as that of Example 70.

Melting point:	194 to 195°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	398 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.36 (3H, s), 3.81 (3H, s), 7.03 (2H, d, J=8.8Hz), 7.07 (1H, dd, J=1.6, 8.0Hz), 7.12 (1H, dt, J=1.6, 8.0Hz), 7.20-7.27 (1H, m), 7.36 (IH, d, J=4.8Hz), 7.58 (2H, d, J=8.8Hz), 7.76-7.83 (IH, m), 8.55-8.61 (2H, m), 9.39 (1H, br-s), 9.65 (1H, br-s)

Elementary analysis for $C_{20}H_{19}N_3O_4S$:			
	C	H	N
Calculated	60.44	4.82	10.57
Found	60.29	4.83	10.49

Example 73

4-[[3-(4-Methoxybenzenesulfonamido)-2-pyridyl]amino]-phenyl β-D-glucopyranoside:



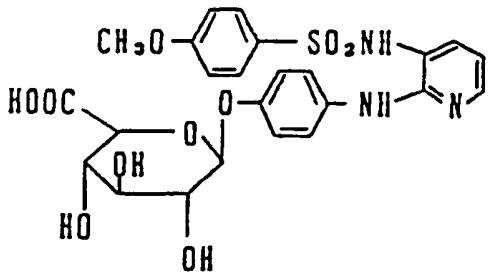
637 mg (0.908 mmol) of the compound produced in Production Example 11 was dissolved in a mixture of 7 ml of

1 N sodium hydroxide and 20 ml of ethanol and the solution was refluxed for 3 h. After cooling, 4 ml of 1 N hydrochloric acid was added to the solution and the mixture was concentrated. Ethyl acetate and water were added to the concentrate and the ethyl acetate layer thus formed was separated, dried, concentrated and purified by silica gel column chromatography to obtain 270 mg of the title compound.

^{1}H-NMR (DMSO-d_6+D_2O) δ (ppm): 3.15-3.33 (4H, m), 3.49 (1H, dd, J=5.6, 11.6Hz), 3.70-3.73 (4H, s+dd), 4.75 (1H, d, J=7.6Hz), 6.68 (1H, dd, J=4.8, 8.0Hz), 6.93 (2H, d, J=9.2Hz), 6.97 (2H, d, J=9.2Hz), 7.23 (1H, dd, J=2.0, 7.6Hz), 7.29 (2H, d, J=9.2Hz), 7.60 (2H, d, J=9.2Hz), 7.95 (1H, dd, J=2.0, 4.8Hz)

Example 74

4-[[3-(4-Methoxybenzenesulfonamido)-2-pyridyl]amino]phenyl β-D-glucopyranoside uronate:

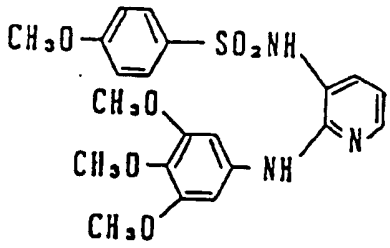


The title compound was produced in the same manner as that of Production Example 11 and Example 73.

^{1}H-NMR (DMSO-D_6+D_2O) δ (ppm): 3.27 (1H, t, J=8.8Hz), 3.33 (1H, t, J=8.8Hz), 3.42 (1H, t, J=8.8Hz), 3.71 (3H, s), 3.86 (1H, d, J=9.6Hz), 4.92 (1H, d, J=7.6Hz), 6.70 (1H, dd, J=5.2, 7.6Hz), 6.90 (2H, d, J=8.8Hz), 6.96 (2H, d, J=8.8Hz), 7.25 (1H, dd, J=1.6, 7.6Hz), 7.29 (2H, d, J=8.8Hz), 7.59 (2H, d, J=8.8Hz), 7.95 (1H, dd, J=1.6, 5.2Hz)

Example 75

4-Methoxy-N-[2-[(3,4,5-trimethoxyphenyl)amino]-3-pyridyl]benzenesulfonamide:



The title compound was produced in the same manner as that of Example 1.

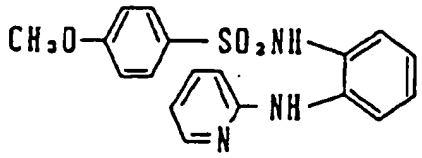
FAB mass spectrometry m/z: 445 (M^+)

^{1}H-NMR (DMSO-d_6) δ (ppm): 3.61 (3H, s), 3.71 (3H, s), 3.74 (6H, s), 6.72 (1H, dd, J=4.8, 7.6Hz), 6.79, 6.80 (2H, s+s), 6.98 (2H, d, J=8.8Hz), 7.24 (1H, dd, J=1.6, 7.6Hz), 7.59 (2H, d, J=8.8Hz), 7.81 (1H, br-s), 8.00 (1H, dd, J=1.6, 4.8Hz), 9.47 (1H, br-s)

Elementary analysis for $C_{21}H_{23}N_3O_6S$:			
	C	H	N
Calculated	56.62	5.20	9.43
Found	56.42	5.22	9.14

Example 76

4-Methoxy-N-[2-[(2-pyridyl)amino]phenyl]benzenesulfonamide:



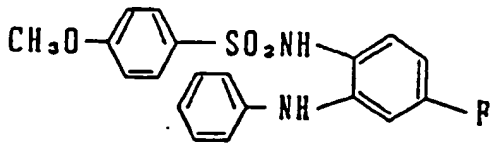
The title compound was produced in the same manner as that of Example 1.

Melting point: 113 to 116°C (recrystallized from cyclohexane)
FAB mass spectrometry m/z: 356 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.70 (3H, s), 6.53-6.59 (1H, m), 6.70-6.75 (1H, m), 6.71 (2H, d, J=8.8Hz), 6.95 (1H, dt, J=1.2, 8.0Hz), 7.11 (1H, dd, J=1.2, 8.0Hz), 7.14 (1H, dt, J=1.6, 8.0Hz), 7.41-7.52 (3H, m), 7.61-7.66 (1H, m), 8.05 (1H, dd, J=1.2, 4.8Hz), 8.06 (1H, br-s), 9.59 (1H, br-s)

Elementary analysis for $C_{18}H_{17}N_3O_3S$:			
	C	H	N
Calculated	60.83	4.82	11.82
Found	61.11	4.82	11.85

Example 77

N-(2-Anilino-4-fluorophenyl)-4-methoxybenzenesulfonamide:



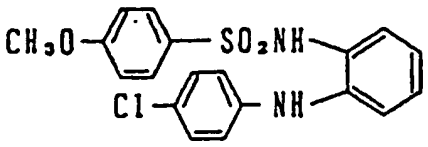
The title compound was produced in the same manner as that of Example 1.

Melting point: 173 to 174°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 372 (M$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.69 (3H, s), 6.57 (1H, dt, J=2.8, 8.8Hz), 6.73-6.91 (6H, m), 7.00 (1H, dd, J=6.4, 8.8Hz), 7.19 (2H, t, J=7.6Hz), 7.37 (1H, br-s), 7.50 (2H, d, J=8.8Hz), 9.33 (1H, br-s)

Elementary analysis for $C_{19}H_{17}FN_2O_3S$:			
	C	H	N
Calculated	61.28	4.60	7.52
Found	61.39	4.62	7.25

Example 78

N-[2-[(4-Chlorophenyl)amino]phenyl]-4-methoxybenzenesulfonamide:



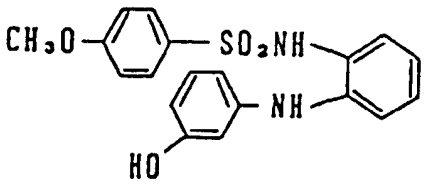
The title compound was produced in the same manner as that of Example 1.

Melting point: 127 to 128°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 388 (M^+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.69 (3H, s), 6.61 (2H, d, J=8.8Hz), 6.77 (2H, d, J=9.2Hz), 6.88-6.94 (1H, m), 7.07-7.14 (4H, m), 7.18 (1H, dd, J=1.2, 8.0Hz), 7.36 (1H, br-s), 7.47 (2H, d, J=9.2Hz), 9.28 (1H, br-s)

Elementary analysis for $C_{19}H_{17}ClN_2O_3S$:			
	C	H	N
Calculated	58.68	4.41	7.20
Found	58.85	4.39	7.04

Example 79

N-[2-[(3-Hydroxyphenyl)amino]phenyl]-4-methoxybenzenesulfonamide:



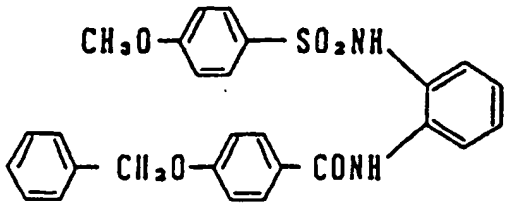
The title compound was produced in the same manner as that of Example 1.

Melting point: 165 to 166°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 370 (M^+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.71 (3H, s), 6.12-6.17 (2H, m), 6.19-6.24 (1H, m), 6.79-6.86 (3H, m), 6.91 (1H, t, J=8.4Hz), 7.07 (1H, dt, J=1.2, 8.0Hz), 7.08 (1H, dd, J=1.2, 8.0Hz), 7.13 (1H, dd, J=1.2, 8.0Hz), 7.14 (1H, br-s), 7.52 (2H, d, J=8.8Hz), 9.16 (1H, s), 9.28 (1H, br-s)

Elementary analysis for $C_{19}H_{18}N_2O_4S$:			
	C	H	N
Calculated	61.61	4.90	7.56
Found	61.62	4.91	7.42

Example 80

4-Benzyloxy-N-[2-(4-methoxybenzenesulfonamido)phenyl]benzamide:



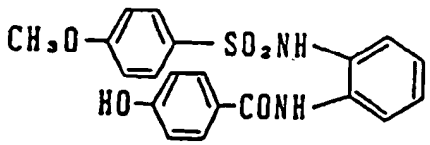
The title compound was produced in the same manner as that of Example 70.

Melting point: 148 to 149°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 489 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.74 (3H, s), 5.23 (2H, s), 6.89 (2H, d, J=8.8Hz), 7.07 (1H, dd, J=2.0, 8.0Hz), 7.10 (1H, dt, J=1.2, 8.0Hz), 7.17 (2H, d, J=8.8Hz), 7.23 (1H, dt, J=2.0, 8.0Hz), 7.33-7.39 (1H, m), 7.42 (2H, t, J=7.6Hz), 7.47-7.52 (4H, m), 7.74 (1H, dd, J=1.2, 8.0Hz), 7.81 (2H, d, J=8.8Hz), 9.44 (1H, br-s), 9.47 (1H, br-s)

Elementary analysis for $C_{27}H_{24}N_2O_5S$:			
	C	H	N
Calculated	66.38	4.95	5.73
Found	66.34	4.92	5.73

Example 81

4-Hydroxy-N-[2-(4-methoxybenzenesulfonamido)phenyl]benzamide:



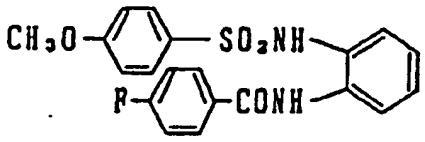
The title compound was produced by catalytically reducing the compound produced in Example 80 in an ordinary manner.

Melting point: 205 to 207°C (recrystallized from ethyl acetate)
FAB mass spectrometry m/z: 399 ($[M+H]^+$)
^{1}H-NMR(DMSO-d_6) δ (ppm): 3.76 (3H, s), 6.89 (2H, d, J=8.8Hz), 6.91 (2H, d, J=8.8Hz), 7.04 (1H, dd, J=1.6, 8.0Hz), 7.09 (1H, dt, J=1.6, 8.0Hz), 7.20-7.25 (1H, m), 7.50 (2H, d, J=8.8Hz), 7.68-7.76 (3H, m), 9.38 (1H, s), 9.47 (1H, s), 10.20 (1H, s)

Elementary analysis for $C_{20}H_{18}N_2O_5S$:			
	C	H	N
Calculated	60.29	4.55	7.03
Found	60.38	4.58	6.75

Example 82

4-Fluoro-N-[2- (4-methoxybenzenesulfonamido)phenyl]-benzamide:



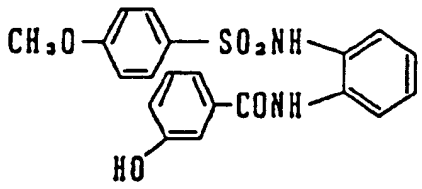
The title compound was produced in the same manner as that of Example 70.

Melting point: 169 to 170°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 401 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.75 (3H, s), 6.90 (2H, d), 7.07-7.16 (2H, m), 7.19-7.26 (IH, m), 7.39 (2H, t, J=8.8Hz), 7.50 (2H, d, J=8.8Hz), 7.66-7.73 (1H, m), 7.91 (2H, dd, J=5.6, 8.8Hz), 9.38 (1H, br-s), 9.54 (1H, br-s)

Elementary analysis for $C_{20}H_{17}FN_2O_4S$:			
	C	H	N
Calculated	59.99	4.28	7.00
Found	60.00	4.31	6.70

Example 83

3-Hydroxy-N-[2- (4-methoxybenzenesulfonamido)phenyl]-benzamide:



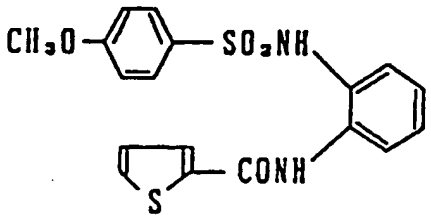
The title compound was produced in the same manner as that of Example 81.

Melting point: 191 to 192°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 399 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.77 (3H, s), 6.92 (2H, d, J=8.8Hz), 6.99-7.06 (2H, m), 7.09 (1H, dt, J=1.6, 8.0Hz), 7.20-7.27 (3H, m), 7.34 (1H, t, J=8.0Hz), 7.51 (2H, d, J=8.8Hz), 7.75-7.81 (1H, m), 9.46 (1H, s), 9.51 (1H, s), 9.81 (1H, s)

Elementary analysis for $C_{20}H_{18}N_2O_5S$:			
	C	H	N
Calculated	60.29	4.55	7.03
Found	60.41	4.55	6.71

Example 84

N-[2-(4-Methoxybenzenesulfonamido)phenyl]-2-thiophenecarboxamide :



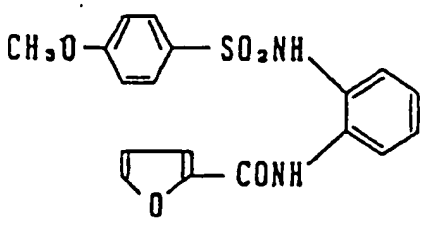
The title compound was produced in the same manner as that of Example 70.

Melting point: 136 to 137°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 389 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.75 (3H, s), 6.85 (2H, d, J=8.8Hz), 7.05-7.13 (2H, m), 7.17-7.26 (2H, m), 7.49 (2H, d, J=8.8Hz), 7.60-7.70 (1H, m), 7.77 (1H, dd, J=1.6, 4.0Hz), 7.87 (1H, dd, J=1.6, 5.2Hz), 9.50 (2H, br-s)

Elementary analysis for $C_{18}H_{16}N_2O_4S_2$:			
	C	H	N
Calculated	55.65	4.15	7.21
Found	55.80	4.27	7.24

Example 85

N-[2-(4-Methoxybenzenesulfonamido)phenyl]-2-furancarboxamide:



The title compound was produced in the same manner as that of Example 70.

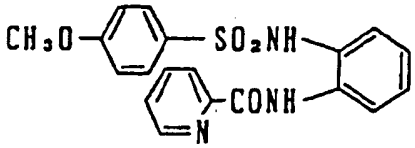
Melting point: 158 to 159°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 373 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.76 (3H, s), 6.73 (1H, dd, J=1.6, 3.6Hz), 6.91 (2H, d, J=8.8Hz), 6.98 (1H,

dd, J=1.6, 8.0Hz), 7.08 (1H, dt, J=1.6, 8.0Hz), 7.21 (1H, dd, J=0.8, 3.6Hz), 7.24 (1H, dt, J=1.6, 8.0Hz), 7.53 (2H, d, J=8.8Hz), 7.84 (1H, dd, J=1.6, 8.0Hz), 7.99 (1H, dd, J=0.8, 1.6Hz), 9.42 (1H, br-s), 9.62 (1H, br-s)

Elementary analysis for $C_{18}H_{16}N_2O_5S$:			
	C	H	N
Calculated	58.05	4.33	7.52
Found	58.08	4.39	7.44

Example 86

N-[2-(4-Methoxybenzenesulfonamido)phenyl]-2-pyridinecarboxamide:



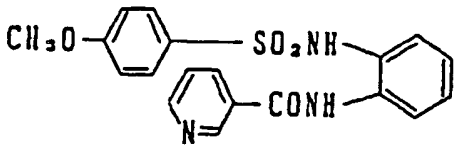
The title compound was produced in the same manner as that of Example 70.

Melting point: 174 to 175°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 384 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.75 (3H, s), 6.82 (1H, dd, J=1.6, 8.0Hz), 6.92 (2H, d, J=8.8Hz), 7.03 (1H, dt, J=1.6, 8.0Hz), 7.30 (1H, dt, J=1.6, 8.0Hz), 7.57 (2H, d, J=8.8Hz), 7.70 (1H, td, J=1.6, 4.8, 7.6Hz), 8.08 (1H, dt, J=1.6, 7.6Hz), 8.12-8.17 (1H, m), 8.24 (1H, dd, J=1.6, 7.6Hz), 8.77 (1H, dd, J=1.6, 4.8Hz), 9.73 (1H, br-s), 10.67 (1H, br-s)

Elementary analysis for $C_{19}H_{17}N_3O_4S$:			
	C	H	N
Calculated	59.52	4.47	10.96
Found	59.73	4.54	10.92

Example 87

N-[2-(4-Methoxybenzenesulfonamido)phenyl]nicotinamide:



The title compound was produced in the same manner as that of Example 70.

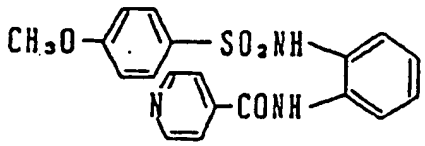
Melting point: 179 to 180°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 384 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.74 (3H, s), 6.89 (2H, d, J=8.8Hz), 7.12-7.19 (2H, m), 7.19-7.27 (1H, m),

7.51 (2H, d, J=8.8Hz), 7.59 (1H, dd, J=4.8, 8.0Hz), 7.63-7.71 (1H, m), 8.17 (1H, dd, J=1.2, 8.0Hz), 8.79 (1H, dd, J=1.2, 4.8Hz), 8.99 (1H, d, J=1.2Hz), 9.49 (1H, br-s), 9.68 (1H, br-s)

Elementary analysis for $C_{19}H_{17}N_3O_4S$:			
	C	H	N
Calculated	59.52	4.47	10.96
Found	59.61	4.57	10.84

Example 88

N-[2-(4-Methoxybenzenesulfonamido)phenyl]isonicotinamide:



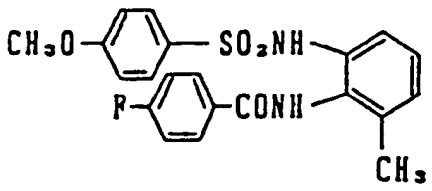
The title compound was produced in the same manner as that of Example 70.

Melting point: 162 to 163°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 384 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.75 (3H, s), 6.90 (2H, d, J=8.8Hz), 7.11-7.27 (3H, m), 7.53 (2H, d, J=8.8Hz), 7.64-7.71 (1H, m), 7.75 (2H, d, J=4.8Hz), 8.81 (2H, d, J=4.8Hz), 9.52 (1H, br-s), 9.73 (1H, br-s)

Elementary analysis for $C_{19}H_{17}N_3O_4S$:			
	C	H	N
Calculated	59.52	4.47	10.96
Found	59.59	4.52	10.96

Example 89

4-Fluoro-N-[2-(4-methoxybenzenesulfonamido)-6-methylphenyl]benzamide:



The title compound was produced in the same manner as that of Example 70.

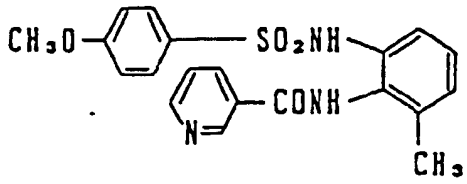
Melting point: 204 to 206°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 415 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 2.10 (3H, s), 3.80 (3H, s), 6.97 (2H, d, J=8.8Hz), 7.00-7.12 (3H, m), 7.37

(2H, t, J=8.8Hz), 7.65 (2H, d, J=8.8Hz), 8.03 (2H, dd, J=5.6, 8.8Hz), 9.46 (1H, br-s), 9.48 (1H, br-s)

Elementary analysis for $C_{21}H_{19}FN_2O_4S$:			
	C	H	N
Calculated	60.86	4.62	6.76
Found	60.74	4.56	6.65

Example 90

N-[2-(4-Methoxybenzenesulfonamido)-6-methylphenyl]nicotinamide:



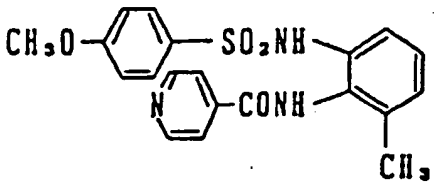
The title compound was produced in the same manner as that of Example 70.

Melting point: 207 to 209°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 398 ($[M+H]^+$)
^{1}H-NMR(DMSO-d_6) δ (ppm): 2.11 (3H, s), 3.79 (3H, s), 6.98 (2H, d, J=8.8Hz), 7.02 (1H, dd, J=1.6, 7.6Hz), 7.05-7.14 (2H, m), 7.58 (1H, dd, J=4.8, 8.0Hz), 7.66 (2H, d, J=8.8Hz), 8.29 (1H, dt, J=1.6, 8.0Hz), 8.77 (1H, dd, J=1.6, 4.8Hz), 9.13 (1H, d, J=1.6Hz), 9.53 (1H, br), 9.64 (1H, br-s)

Elementary analysis for $C_{20}H_{19}N_3O_4S$:			
	C	H	N
Calculated	60.44	4.82	10.57
Found	60.55	4.90	10.53

Example 91

N-[2-(4-Methoxybenzepesulfonamido)-6-methylphenyl]isonicotinamide:



The title compound was produced in the same manner as that of Example 70.

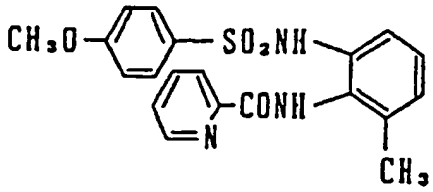
Melting point: 213 to 217°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 398 ($[M+H]^+$)
^{1}H-NMR(DMSO-d_6) δ (ppm): 2.10 (3H, s), 3.80 (3H, s), 6.99 (2H, d, J=8.8Hz), 7.02 (1H, dd, J=1.6, 7.6Hz),

7.04-7.14 (2H, m), 7.67 (2H, d, J=8.8Hz), 7.87 (2H, dd, J=1.6, 8.4Hz), 8.80 (2H, dd, J=1.6, 8.4Hz), 9.56 (1H, br-s), 9.73 (1H, br-s)

Elementary analysis for $C_{20}H_{19}N_3O_4S$:			
	C	H	N
Calculated	60.44	4.82	10.57
Found	60.60	4.85	10.53

Example 92

N-[2-(4-Methoxybenzenesulfonamido)-6-methylphenyl]-2-pyridinecarboxamide:



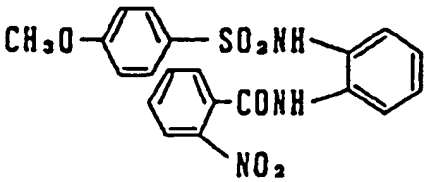
The title compound was produced in the same manner as that of Example 70.

Melting point: 180 to 182°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 398 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 2.12 (3H, s), 3.78 (3H, s), 6.90 (2H, d, J=8.8Hz), 6.93 (1H, t, J=4.8Hz), 7.11 (2H, d, J=4.8Hz), 7.54 (2H, d, J=8.8Hz), 7.65-7.72 (1H, m), 8.03-8.08 (2H, m), 8.75 (1H, dd, J=1.2, 5.2Hz), 9.53 (1H, br-s), 10.11 (1H, br-s)

Elementary analysis for $C_{20}H_{19}N_3O_4S$:			
	C	H	N
Calculated	60.44	4.82	10.57
Found	60.43	4.92	10.45

Example 93

N-[2-(4-Methoxybenzenesulfonamido)phenyl]-2-nitrobenzamide:



The title compound was produced in the same manner as that of Example 70.

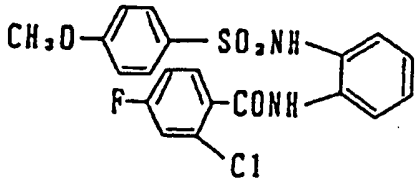
Melting point: 168 to 170°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 428 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.80 (3H, s), 7.05 (2H, d, J=8.8Hz), 7.07-7.16 (2H, m), 7.19-7.26 (1H, m),

7.62 (2H, d, J=8.8Hz), 7.66 (1H, d, J=8.0Hz), 7.73 (1H, d, J=8.0Hz), 7.79 (1H, t, J=8.0Hz), 7.92 (1H, t, J=8.0Hz), 8.16 (1H, d, J=8.0Hz), 9.23 (1H, br-s), 9.93 (1H, br-s)

Elementary analysis for $C_{20}H_{17}N_3O_6S$:			
	C	H	N
Calculated	56.20	4.01	9.83
Found	56.21	4.05	9.77

Example 94

2-Chloro-4-fluoro-N-[2-(4-methoxybenzenesulfonamido)phenyl]benzamide:



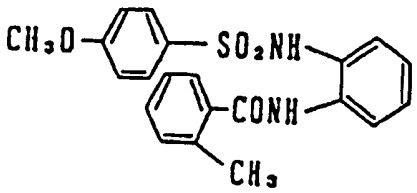
The title compound was produced in the same manner as that of Example 70.

Melting point: 160 to 162°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 435 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.81 (3H, s), 6 97-7.18 (4H, m), 7.19-7.28 (1H, m), 7.34-7.44 (1H, m), 7.51-7.64 (4H, m), 6.74-7.82 (1H, m), 9.33 (1H, br-s), 9.69 (1H, s)

Elementary analysis for $C_{20}H_{16}ClN_2O_4S$:			
	C	H	N
Calculated:	55.24	3.71	6.44
Found:	55.42	3.90	6.20

Example 95

N-[2-(4-Methoxybenzenesulfonamido)phenyl]-2-methylbenzamide:



The title compound was produced in the same manner as that of Example 70.

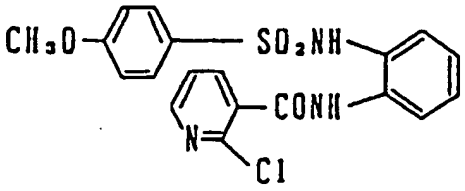
Melting point: 129 to 130°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 397 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 2.38 (3H, s), 3.81 (3H, s), 7.03 (2H, d, J=8.8Hz), 7.07 (1H, dd, J=2.0, 8.0Hz), 7.10 (1H, dt, J=1.2, 8.0Hz), 7.19-7.27 (1H, m), 7.27-7.39 (3H, m), 7.42 (1H,

dt, J=2.0, 7.2Hz), 7.56 (2H, d, J=8.8Hz), 7.80-7.87 (lH, m), 9.40 (1H, br-s), 9.46 (1H, br-s)

Elementary analysis for $C_{21}H_{20}N_2O_4S$:			
	C	H	N
Calculated	63.62	5.09	7.07
Found	63.64	5.09	7.03

Example 96

2-Chloro-N- [2- (4-methoxybenzenesulfonamido)phenyl]-nicotinamide:



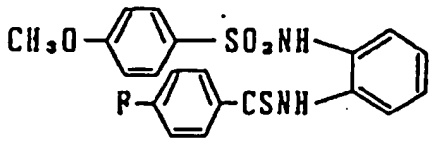
The title compound was produced in the same manner as that of Example 70.

Melting point: 133 to 135°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 418 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.81 (3H, s), 7.04 (2H, d, J=8.8Hz), 7.07-7.15 (2H, m), 7.18-7.22 (1H, m), 7.60 (2H, d, J=8.8Hz), 7.61 (1H, dd, J=4.8, 7.6Hz), 7.78 (1H d, J=7.6Hz), 7.98 (lH, dd, J=2.0, 7.6Hz), 8.56 (lH, dd, J=2.0, 4.8Hz), 9.29 (1H, br-s), 9.87 (1H, s)

Elementary analysis for $C_{19}H_{16}ClN_3O_4S$:			
	C	H	N
Calculated	54.61	3.86	10.06
Found	54.71	3.87	9.90

Example 97

4-Fluoro-N-[2- (4-methoxybenzenesulfonamido)phenyl]-benzothioamide:



A mixture of 549 mg (1.371 mmol) of the compound produced in Example 82, 333 mg (0.823 mmol) of Lawesson reagent and 10 ml of toluene was heated at 100°C. After the concentration, the residue was purified by silica gel column chromatography to obtain 506 mg of the title compound.

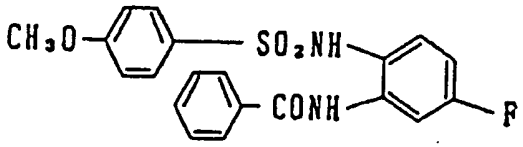
Melting point: 155 to 156°C (recrystallized from n-butanol)
FAB mass spectrometry m/z: 417 ([M+H]+)

^{1}H-NMR (DMSO-d_6) δ (ppm): 3.80 (3H, s), 7.02 (2H, d, J=8.8Hz), 7.10-7.25, (3H, m), 7.33 (2H, t, J=8.8Hz), 7.47-7.58 (1H, m), 7.63 (2H, d, J=8.8Hz), 7.98 (2H, dd, J=5.6, 8.8Hz), 9.45 (1H, br), 11.13 (1H, br)

Elementary analysis for $C_{20}H_{17}FN_2O_3S_2$:			
	C	H	N
Calculated	57.68	4.11	6.73
Found	57.63	4.12	6.58

Example 98

N-[5-fluoro-2-(4-methoxybenzenesulfonamido)phenyl]benzamide:



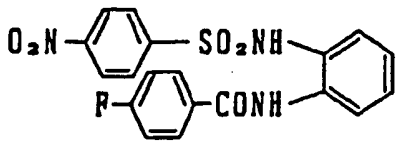
The title compound was produced in the same manner as that of Example 70.

Melting point: 153 to 154°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 401 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.75 (3H, s), 6.88 (2H, d, J=8.8Hz), 6.94 (1H, dt, J=3.2, 8.8Hz), 7.00 (1H, dd, J=6.0, 8.8Hz), 7.47 (2H, d, J=8.8Hz), 7.55 (2H, t, J=7.6Hz), 7.59-7.66 (1H, m), 7.74-7.83 (3H, m), 9.45 (1H, br-s), 9.55 (1H, br-s)

Elementary analysis for $C_{20}H_{17}FN_2O_4S$:			
	C	H	N
Calculated	59.55	4.28	7.00
Found	59.97	4.32	6.79

Example 99

4-Fluoro-N-[2-(4-nitrobenzenesulfonamido)phenyl]benzamide:



The title compound was produced from the compound produced in Production Example 13 in the same manner as that of Example 70.

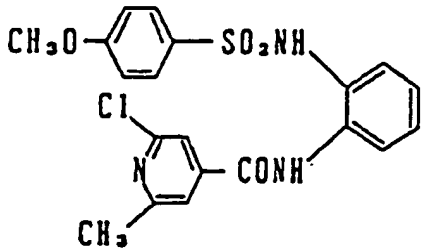
Melting point: 265 to 266°C (recrystallized from ethyl acetate)
FAB mass spectrometry m/z: 416 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 7.21 (1H, dt, J=1.6, 8.0Hz), 7.25 (1H, dd, J=2.0, 8.0Hz), 7.30 (1H, dt, J=2.0, 8.0Hz), 7.35 (2H, t, J=8.8Hz), 7.55-7.60 (1H, m), 7.76 (2H, d, J=8.8Hz), 7.83

(2H, dd, J=5.6, 8.8Hz), 8.22 (2H, d, J=8.8Hz), 9.42 (1H, s), 9.89 (1H, s)

Elementary analysis for $C_{19}H_{14}FN_3O_5S$:			
	C	H	N
Calculated	54.94	3.40	10.12
Found	54.90	3.36	9.93

Example 100

2-Chloro-6-methyl-N- [2- (4-methoxybenzenesulfonamido)-phenyl]isonicotinamide:



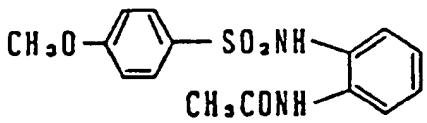
The title compound was produced in the same manner as that of Example 70.

Melting point: 150 to 151°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 432 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (pom): 2.58 (3H, s), 3.76 (3H, s), 6.90 (2H, d, J=8.8Hz), 7.15-7.26 (3H, m), 7.52 (2H, d, J=8.8Hz), 7.54-7.63 (3H, m), 9.44 (1H, br-s), 9.73 (1H, br-s)

Elementary analysis for $C_{20}H_{18}ClN_3O_4S$:			
	C	H	N
Calculated	55.62	4.20	9.73
Found	55.80	4.26	9.75

Example 101

N-[2-(4-Methoxybenzenesulfonamido)phenyl]acetamide:



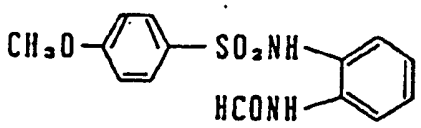
The title compound was produced in the same manner as that of Example 70.

Melting point: 160 to 161°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 321 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 1.96 (3H, s), 3.80 (3H, s), 6.99-7.17 (5H, m), 7.48 (1H, d, J=8.0Hz), 7.53 (2H, d, J=8.8Hz), 9.23 (2H, br-s)

Elementary analysis for $C_{15}H_{16}N_2O_4S$:			
	C	H	N
Calculated	56.24	5.03	8.75
Found	56.26	5.03	8.72

Example 102

N-[2-(4-Methoxybenzenesulfonamido)phenyl]formamide:



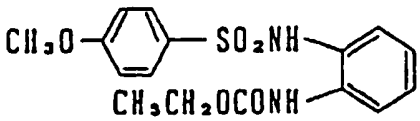
The title compound was produced in the same manner as that of Example 70.

Melting point: 143 to 144°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 307 ($[M+H]^+$)

Elementary analysis for $C_{14}H_{14}N_2O_4S$:			
	C	H	N
Calculated	54.89	4.61	9.14
Found	55.05	4.65	9.09

Example 103

N- [2-[(Ethoxycarbonyl)amino]phenyl] -4-methoxybenzenesulfonamide:



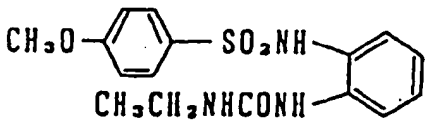
The title compound was produced in the same manner as that of Example 70.

Melting point: 118 to 119°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 351 ($[M+H]^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 1.22 (3H, t, J=7.2Hz), 3.79 (3H, s), 4.03 (2H, q, J=7.2Hz), 6.98-7.03 (4H, m), 7.17 (1H, t, J=8.0Hz), 7.52 (2H, d, J=8.8Hz), 7.57 (1H, d, J=8.0Hz), 8.43 (1H, s), 9.35 (1H, s)

Elementary analysis for $C_{16}H_{18}N_2O_5S$:			
	C	H	N
Calculated	54.84	5.18	7.99
Found	54.78	5.19	7.86

Example 104

N-[2-[(Ethylaminocarbonyl)amino]phenyl]-4-methoxybenzenesulfonamide:



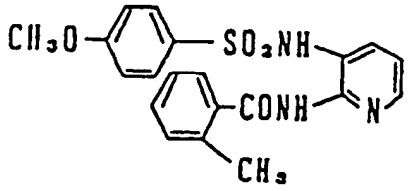
The title compound was produced by reacting the compound produced in Production Example 12 with ethyl isocyanate and treating the product in an ordinary manner.

Melting point:	152 to 154°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	350 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	1.08 (3H, t, J=7.2Hz), 3.10 (2H, dq, J=5.6, 7.2Hz), 3.82 (3H, s), 6.61 (1H, dd, J=1.6, 8.0Hz), 6.77 (1H, dt, J=1.2, 8.0Hz), 6.89 (1H, t, J=5.6Hz), 7.04 (2H, d, J=8.8Hz), 7.05-7.12 (1H, m), 7.57 (2H, d, J=8.8Hz), 7.78 (1H, dd, J=1.2, 8.4Hz), 7.94 (1H, s), 9.41 (1H, s)

Elementary analysis for $C_{16}H_{19}N_3O_4S$:			
	C	H	N
Calculated	55.00	5.48	12.03
Found	55.08	5.47	11.88

Example 105

N-[3-(4-Methoxybenzenesulfonamido)-2-pyridyl]-2-methylbenzamide:



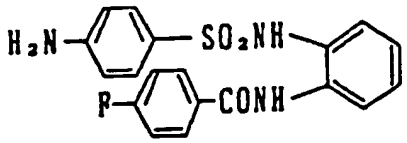
The title compound was produced in the same manner as that of Example 70.

Melting point:	160 to 162°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	398 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm):	2.37 (3H, s), 3.81 (3H, s), 7.05 (2H, d, J=8.8Hz), 7.22-7.33 (4H, m), 7.36-7.43 (1H, m), 7.59 (2H, d, J=8.8Hz), 7.71 (1H, dd, J=1.6, 8.0Hz), 8.25 (1H, dd, J=1.6, 4.8Hz), 9.24 (1H, br-s), 10.47 (1H, br-s)

Elementary analysis for $C_{20}H_{19}N_3O_4S$:			
	C	H	N
Calculated	60.44	4.82	10.57
Found	60.53	4.84	10.67

Example 106

N-[2-(4-Aminobenzenesulfonamido)phenyl]-4-fluorobenzamide:



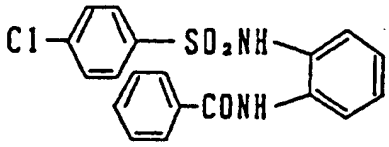
The title compound was produced by reducing the compound produced in Example 99 with zinc/hydrochloric acid.

Melting point:	203 to 205°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	386 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm):	5.98 (2H, br-s), 6.45 (2H, d, J=8.8Hz), 7.05 (1H, dd, J=1.6, 8.0Hz), 7.09 (1H, dt, J=1.6, 8.0Hz), 7.20 (1H, dt, J=1.6, 8.0Hz), 7.23 (2H, d, J=8.8Hz), 7.39 (2H, t, J=8.8Hz), 7.74-7.80 (1H, m), 7.93 (2H, dd, J=5.6, 8.8Hz), 9.20 (1H, br-s), 9.63 (1H, br-s)

Elementary analysis for $C_{19}H_{16}FN_3O_3S$:			
	C	H	N
Calculated	59.21	4.18	10.90
Found	59.36	4.21	10.80

Example 107

N-[2-(4-Chlorobenzenesulfonamido)phenyl]benzamide



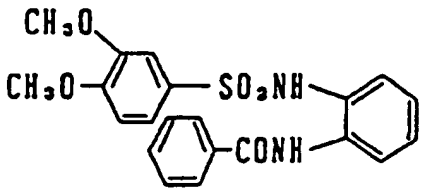
The title compound was produced in the same manner as that of Example 70.

Melting point:	191 to 192°C (recrystallized from ethanol)
FAB mass spectrometry m/z:	387 ([M+H]+)
^{1}H-NMR (DMSO-d_6) δ (ppm):	7.13-7.20 (2H, m), 7.24-7.30 (1H, m), 7.42 (2H, d, J=8.8Hz), 7.54 (2H, d, J=8.8Hz), 7.55 (2H, t, J=8.8Hz), 7.60-7.66 (1H, m), 7.68-7.72 (1H, m), 7.78-7.83 (2H, m), 9.52 (1H, s), 9.71 (1H, s)

Elementary analysis for $C_{19}H_{15}ClN_2O_3S$:			
	C	H	N
Calculated	58.99	3.91	7.24
Found	59.25	4.02	7.29

Example 108

N-[2-(3,4-Dimethoxybenzenesulfonamido)phenyl]benzamide:



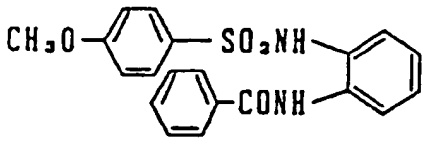
The title compound was produced in the same manner as that of Example 70.

Melting point: 183 to 184°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 413 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.53 (3H, s), 3.75 (3H, s), 6.90 (1H, d, J=8.4Hz), 6.95 (1H, d, J=2.0Hz), 7.13 (1H, dd, J=2.0, 8.4Hz), 7.13-7.18 (2H, m), 7.23-7.29 (1H, m), 7.54 (2H, t, J=7.6Hz), 7.59-7.65 (1H, m), 7.71-7.76 (1H, m), 7.76-7.82 (2H, m), 9.43 (1H, br-s), 9.53 (1H, br-s)

Elementary analysis for $C_{21}H_{20}N_2O_5S$:			
	C	H	N
Calculated	61.15	4.89	6.79
Found	61.16	4.90	6.82

Example 109

N-[2-(4-Methoxybenzenesulfonamido)phenyl]benzamide:



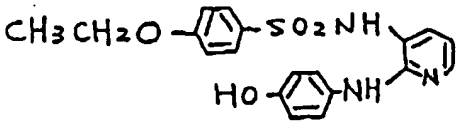
The title compound was produced in the same manner as that of Example 70.

Melting point: 167 to 168°C (recrystallized from ethanol)
FAB mass spectrometry m/z: 383 ([M+H]$^+$)
^{1}H-NMR (DMSO-d_6) δ (ppm): 3.75 (3H, s), 6.91 (2H, d, J=8.8Hz), 7.08 (1H, dd, J=1.6, 8.0Hz), 7.12 (1H, dt, J=1.6, 8.0Hz), 7.24 (1H, dt, J=1.6, 8.0Hz), 7.51 (2H, d, J=8.8Hz), 7.52-7.59 (2H, m), 7.60-7.66 (1H, m), 7.76 (1H, dd, J=1.6, 8.0Hz), 7.81-7.86 (2H, m), 9.50 (1H, br-s), 9.55 (1H, br-s)

Elementary analysis for $C_{20}H_{18}N_2O_4S$:			
	C	H	N
Calculated	62.81	4.74	7.33
Found	63.06	4.77	7.32

Example 110

4-ethoxy-N-[2-((4-hydroxyphenyl)amino) -3-pyridyl]-benzenesulfoneamide was prepared.



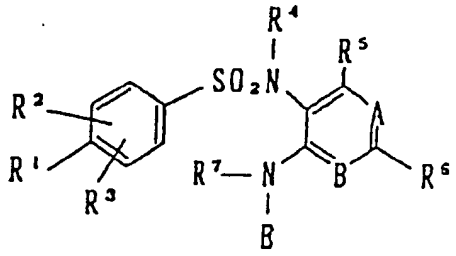
melting point: 194-195°c (recrystalized from ethanol)
FAB mass analysis m/z: 386 ([M+H]$^+$)

elementary analysis as C19H19N303S			
	C	H	N
calculated	59.21	4.97	10.90
found	59.12	4.93	10.66

^{1}H-NMR (DMSO-d_6) δ (ppm):
1.27 (3H, t, J=7.2Hz), 3.98 (2H, g, J=7.2Hz), 6.59 (1H, dd, J=4.8, 7.6Hz), 6.61 (2H, d, J=8.8Hz), 6.95 (2H, d, J=9.2Hz), 7.12 (2H, d, J=8.8Hz) 7.17 (1H, dd, J=1.6, 7.6Hz), 7.55 (1H, br-s), 7.56 (2H, d, J=9.2Hz), 7.87 (1H, dd, J=1.6-4.8Hz) 8.97 (1H, s), 9.41 (1H, br-s)

Claims

1. Sulfonamide derivatives of the general formula (I) or pharmacologically acceptable salts of them:

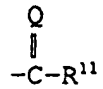


(I)

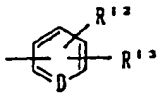
wherein:

R^1 represents a hydrogen atom, halogen atom, C_{1-6} alkyl group, C_{1-6} alkoxy group, hydroxyl group, nitro group, phenoxy group, cyano group, acetyl group or amino group which may be protected,
R^2 and R^3 may be the same or different from each other and each represent a hydrogen atom, halogen atom, C_{1-6} alkyl group or C_{1-6} alkoxy group,
R^4 and R^7 may be the same or different from each other and each represent a hydrogen atom or C_{1-6} alkyl group,
R^5 and R^6 may be the same or different from each other and each represent a hydrogen atom, halogen atom, C_{1-6} alkoxy group or amino group which may be substituted,
A represents a group of the formula: =N- or =CH-,
B represents a group of the formula: =N- or

in which R^{10} represents a hydrogen atom or C_{1-6} alkyl group,
E represents a group of the formula:



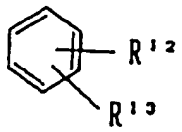
in which Q represents an oxygen atom or sulfur atom and R^{11} represents a hydrogen atom, C_{1-6} alkyl group, amino group which may be substituted with a C_{1-6} alkyl group, C_{1-6} alkoxy group, 2-thienyl group, 2-furyl group or group of the formula:



(D being a group of the formula: =N- or =CH- and R^{12} and R^{13} being the same or different from each other and each being a hydrogen atom, halogen atom, nitro group, hydroxyl group which may be protected or C_{1-6} alkyl group); or an aromatic 6-membered cyclic group which may be substituted with 1 to 3 substituents G which may be the same or different from one another and which cyclic group may have 1 or 2 nitrogen atoms in the ring (G being a halogen atom, C_{1-6} alkyl group, C_{1-6} alkoxy group, hydroxyl group which may be protected, carboxyl group which may be esterified or amidated, C_{1-6} alkylthio group or phenoxy group, with the proviso that the following combinations are excluded:

(1) a combination of R^1 which is a hydrogen atom, C_{1-6}alkyl group, nitro group or amino group which may be protected, R^2 and R^3 which are each a hydrogen atom, A and B which are each =CH- and E which is a phenyl group which may be substituted with 1 to 3 substituents G which may be the same or different from one another, and
(2) a combination of R^1, R^2 and R^3 which may be the same or different from one another and which are each a hydrogen atom, C_{1-6} alkyl group, nitro group, halogen atom, or acetylamino group, A and B which are each =CH-,
and E which is a group of the formula:

in which R^{11} is a C_{1-6} alkyl group, amino group which may be substituted with a C_{1-6} alkyl group or a group of the formula:



(R^{12} and R^{13} being each as defined above).

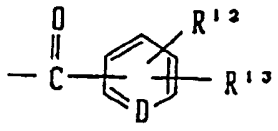
2. Sulfonamide derivatives or pharmacologically acceptable salts of them according to Claim 1, wherein R^1 represents a C_{1-6} alkoxy group.

3. Sulfonamide derivatives or pharmacologically acceptable salts of them according to Claim 1 wherein A represents a group of the formula: =CH- and B represents a group of the formula: =N-.

4. Sulfonamide derivatives or pharmacologically acceptable salts of them according to any of Claims 1 to 3, wherein E represents a phenyl group, pyridyl group or pyrimidyl group which may be substituted with 1 to 3 same or different substituents G (G being as defined in Claim 1).

5. Sulfonamide derivatives or pharmacologically acceptable salts of them according to any of Claims 1 to 3, wherein E represents a phenyl group substituted with a hydroxyl group which may be protected.

6. Sulfonamide derivatives or pharmacologically acceptable salts of them according to any of Claims 1 to 3, wherein A and B each represent a group of the formula: =CH-,
and E represents a group of the formula:



in which D, R^{12} and R^{13} are each as defined above.

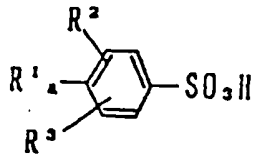
7. Sulfonamide derivatives or pharmacologically acceptable salts of them according to Claim 1 or 2 wherein A represents a group of the formula: =CH-, B represents a group of the formula:

and E represents a group of the formula:

in which R^{11} is as defined in Claim 1.

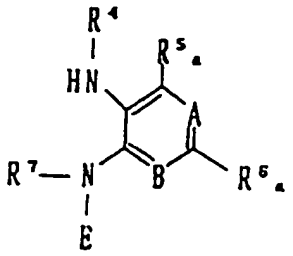
8. A process for producing sulfonamide derivatives or pharmacologically acceptable salts of them according to any one of the claims 1 to 7 by any of the following processes (a) to (d):

(a) a process wherein a sulfonic acid of the general formula (II) or its reactive derivative:



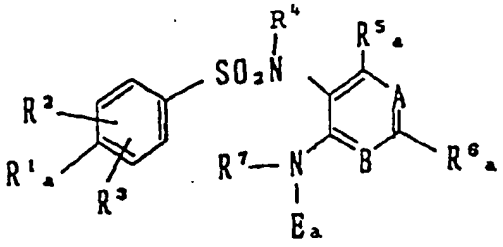
(II)

wherein $R^1{}_a$ represents a hydrogen atom, halogen atom, $C_{1\text{-}6}$ alkyl group, $C_{1\text{-}6}$ alkoxy group, protected hydroxyl group, nitro group, phenoxy group, cyano group, acetyl group or protected amino group, and R^2 and R^3 are as defined in Claim 1,
is reacted with a compound of the general formula (III):



(III)

wherein R^4, R^7, A, B and E are as defined in Claim 1, and $R^5{}_a$ and $R^6{}_a$ may be the same or different from each other and each represent a hydrogen atom, halogen atom, C_{1-6} alkoxy group or protected or substituted amino group,
and when the resultant compound has a protective group, said protective group is removed, if desired,
(b) a process wherein a compound of the general formula (IV)

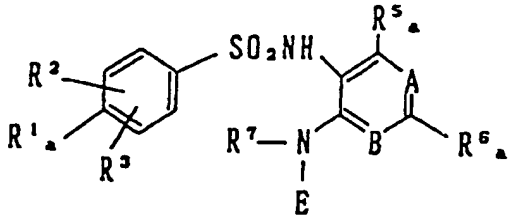


(IV)

wherein $R^1{}_a$, R^2, R^3, R^4, $R^5{}_a$, $R^6{}_a$, R^7, A and B are each as defined above, and Ea represents an aromatic 6-membered cyclic group (which may contain 1 or 2 nitrogen atoms in the ring) substituted with 1 to 3 substituents Ga which may be the same or different from one another, Ga being a halogen atom, C_{1-6} alkyl group, C_{1-6} alkoxy group, hydroxyl group, carboxyl group which may be esterified or amidated, C_{1-6} alkylthio group or phenoxy group with the proviso that at least one Ga on the ring is a hyroxyl group,
is reacted with a compound of the general formula (V):

X-Y (V)

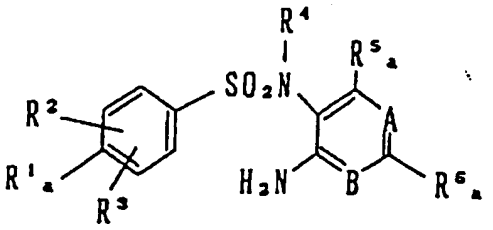
wherein X represents a group capable of bonding with the oxygen atom of the hydroxyl group and Y represents a removable group,
or with an inorganic acid or organic acid anhydride reactive with the hydroxyl group and when the resultant compound has a protective group, said protective group is removed, if desired,
(c) a process wherein a compound of the general formula (VI):



(VI)

wherein $R^1{}_a$, R^2, R^3, $R^5{}_a$, $R^6{}_a$, R^7, A, B and E are each as defined above,
is reacted with an alkylating agent and when the resultant compound has a protective group, said protective group is removed, if desired, and

(d) a process wherein a compound of the general formula (VII):



(VII)

wherein $R^1{}_a$, R^2, R^3, R^4, $R^5{}_a$, $R^6{}_a$, A and B are each as defined above, is reacted with a compound of the general formula (VIII):

$$R^{11}\text{-}Z \qquad \text{(VIII)}$$

wherein R^{11} is as defined above, and Z represents a carboxyl group or its reactive derivative, or when R^{11} is a $C_{1\text{-}6}$ alkylamino group, it is reacted with a $C_{1\text{-}6}$ alkyl isocyanate.

9. An antineoplastic agent comprising a sulfonamide derivative or its pharmacologically acceptable salt according to any one of the claims 1 to 7 as the active ingredient.

10. Sulfonamide derivatives or pharmacologically acceptable salts of them according to any one of the claims 1 to 7 wherein the compound is selected from among the following sulfonamide derivatives:

1) N-(2-anilino-3-pyridyl)-p-toluenesulfonamide,
2) N-(2-anilino-3-pyridyl)-4-ethylbenzenesulfonamide,
3) N-(2-anilino-3-pyridyl)-4-methoxybenzenesulfonamide,
4) 4-methoxy-N-[2-[(4-methoxyphenyl)amino]-3-pyridyl]benzenesulfonamide,
5) N-[2-[(4-hydroxyphenyl)amino]-3-pyridyl]-4-methoxybenzenesulfonamide,
6) 4-methoxy-N-[2-[(4-pyridyl)amino]-3-pyridyl]-benzenesulfonamide,
7) 4-[[3-(4-methoxybenzenesulfonamido)-2-pyridyl]-aminolphenyl dihydrogenphosphate,
8) N-(2-anilinophenyl)-4-methoxybenzenesulfonamide,
9) N-[2-(4-methoxybenzenesulfonamido)phenyl]-2-methylnicotinamide,

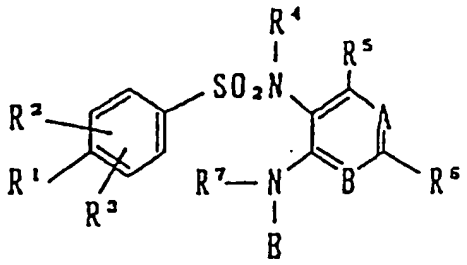
and

10) N-[2-(4-methoxybenzenesulfonamido)phenyl]-3-methylisonicotinamide.

11. A pharmacological composition which comprises a pharmacologically effective amount of the derivative as defined in any one of the claims 1 to 7 and a pharmacologically acceptable carrier.

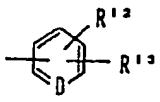
Patentansprüche

1. Sulfonamidderivate der allgemeinen Formel (I) oder pharmakologisch akzeptable Salze davon



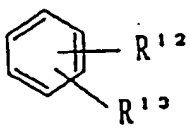
(I)

worin bedeuten:
R^1 ein Wasserstoffatom, Halogenatom, C_{1-6}-Alkylgruppe, C_{1-6}-Alkoxygruppe, Hydroxylgruppe, Nitrogruppe, Phenoxygruppe, Cyanogruppe, Acetylgrupppe oder Aminogruppe, die geschützt sein können, R^2 und R^3, die gleich oder verschieden voneinander sein können, jeweils ein Wasserstoffatom, Halogenatom, C_{1-6}-Alkylgruppe oder C_{1-6}-Alkoxygruppe, R^4 und
R^7, die gleich oder verschieden voneinander sein können, jeweils ein Wasserstoffatom oder eine C_{1-6}-Alkylgruppe, R^5 und R^6, die gleich oder verschieden voneinander sein können, jeweils ein Wasserstoffatom, Halogenatom, C_{1-6}-Alkoxygruppe oder Aminogruppe, die substituiert sein kann, A eine Gruppe der Formel =N- oder =CH-,
B eine Gruppe der Formel: =N- oder =C(R^{10})-, worin R^{10} ein Wasserstoffatom oder C_{1-6}-Alkylgruppe ist, E eine Gruppe der Formel -C(=Q)-R^{11}, worin Q ein Sauerstoffoder Schwefelatom und R^{11} ein Wasserstoffatom, C_{1-6}-Alkylgruppe, Aminogruppe, die substituiert sein kann mit einer C_{1-6}-Alkylgruppe, C_{1-6}-Alkoxygruppe, 2-Thienylgruppe, 2-Furylgruppe oder einer Gruppe der Formel:



worin D eine Gruppe der Formel: =N- oder =CH- und R^{12} und R^{13} gleich oder verschieden voneinander sind und jeweils ein Wasserstoffatom, Halogenatom, Nitrogruppe, Hydroxylgruppe, die geschützt sein kann, oder C_{1-6}-Alkylgruppe sind); oder eine aromatische, 6-gliedrige, zyklische Gruppe, die mit 1 bis 3 Substituenten G substituiert sein kann, die gleich oder verschieden voneinander sein können, und worin die zyklische Gruppe 1 oder 2 Stickstoffatome in dem Ring haben kann (worin G ein Halogenatom, C_{1-6}-Alkylgruppe, C_{1-6}-Alkoxygruppe, Hydroxylgruppe, die geschützt sein kann, Carboxylgrupe, die verestert oder amidiert sein kann, c_{1-6}-Alkylthiogruppe oder Phenoxygruppe ist), mit dem Vorbehalt, daß die folgenden Kombinationen ausgeschlossen sind:

(1) eine Kombination von R^1, das ein Wasserstoffatom, C_{1-6}-Alkylgruppe, Nitrogruppe oder Aminogruppe ist, die geschützt sein kann, R^2 und R^3, die jeweils ein Wasserstoffatom sind, A und B, die jeweils =CH- sind, und E, das eine Phenylgruppe ist, die mit 1 bis 3 Substituenten G substituiert sein kann, die gleich oder verschieden voneinander sein können, und
(2) eine Kombination von R^1, R^2 und R^3, die gleich oder verschieden voneinander sein können, und jeweils ein Wasserstoffatom, C_{1-6}-Alkylgruppe, Nitrogruppe, Halogenatom oder Acetylaminogruppe sind, worin A und B jeweils =CH- sind, und E, das eine Gruppe der Formel: -C(=O)-R^{11} ist, worin R^{11} eine C_{1-6}-Alkylgruppe, Aminogrupe, die mit einer C_{1-6}-Alkylgruppe substituiert sein kann, oder eine Gruppe der Formel ist



(worin R^{12} und R^{13} wie oben definiert sind).

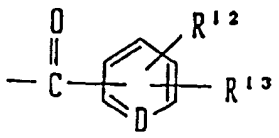
2. Sulfonamidderivate oder pharmakologisch akzeptable Salze davon nach Anspruch 1, worin R^1 eine C_{1-6}-Alkoxygruppe bedeutet.

3. Sulfonamidderivate oder pharmakologisch akzeptable Salze davon nach Anspruch 1, worin A eine Gruppe der Formel =CH-und B eine Gruppe der Formel =N- sind.

4. Sulfonamidderivate oder pharmakologisch akzeptable Salze davon nach einem der Ansprüche 1 bis 3, worin E eine Phenylgruppe, Pyridylgruppe oder Pyrimidylgruppe ist, die mit 1 bis 3 gleichen oder verschiedenen Substituenten G substituiert sein kann (worin G wie in Anspruch 1 definiert ist).

5. Sulfonamidderivate oder pharmakologisch akzeptable Salze davon nach einem der Ansprüche 1 bis 3, worin E eine Phenylgruppe bedeutet, die mit einer Hydroxylgruppe substituiert ist, die geschützt sein kann.

6. Sulfonamidderivate oder pharmakologisch akzeptable Salze davon nach einem der Ansprüche 1 bis 3, worin A und B jeweils eine Gruppe der Formel =CH- sind und E eine Gruppe der Formel ist:

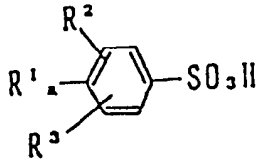


worin D, R^{12} und R^{13} jeweils wie oben definiert sind.

7. Sulfonamidderivate oder pharmakologisch akzeptable Salze davon nach Anspruch 1 oder 2, worin A eine Gruppe der Formel: =CH-, B eine Gruppe der Formel $=C(CH_3)$- und E eine Gruppe der Formel $-C(=O)-R^{11}$ sind, worin R^{11} wie in Anspruch 1 definiert sind.

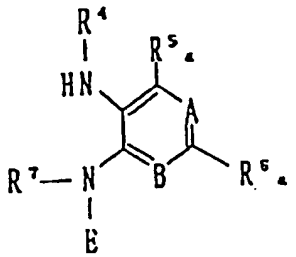
8. Verfahren zur Erzeugung von Sulfonamidderivaten oder pharmakologisch akzeptablen Salzen davon nach einem der Ansprüche 1 bis 7 nach einem der folgenden Verfahren (a) bis (d):

(a) ein Verfahren, worin eine Sulfonsäure der allgemeinen Formel (II) oder deren reaktives Derivat:



(II)

worin $R^1{}_a$ ein Wasserstoffatom, Halogenatom, C_{1-6}-Alkylgruppe, C_{1-6}-Alkoxygruppe, geschützte Hydroxylgruppe, Nitrogruppe, Phenoxygruppe, Cyanogruppe, Acetylgruppe oder geschützte Aminogruppe ist und R^2 und R^3 wie in Anspruch 1 definiert sind, mit einer Verbindung der allgemeinen Formel (III) reagiert wird:

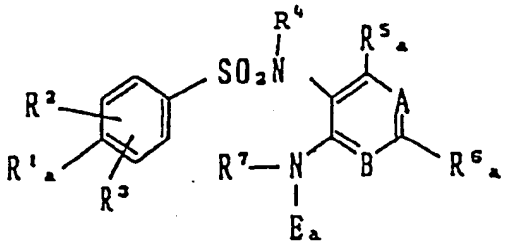


(III)

worin R^4, R^7, A, B und E wie in Anspruch 1 definiert sind und $R^5{}_a$ und $R^6{}_a$ gleich oder verschieden voneinander sein können und jeweils ein Wasserstoffatom, Halogenatom, C_{1-6}-Alkoxygruppe oder geschützte oder substi-

tuierte Aminogruppe sind, und wenn die resultierende Verbindung eine Schutzgruppe aufweist, wird diese Schutzgruppe gegebenenfalls entfernt,

(b) ein Verfahren, worin eine Verbindung der allgemeinen Formel (IV)



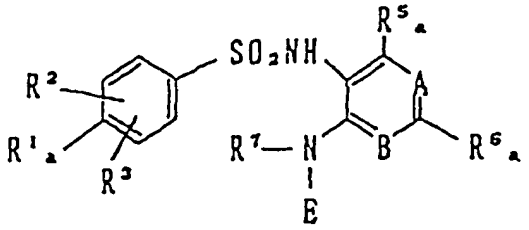
(IV)

worin $R^1{}_a$, R^2, R^3, R^4, $R^5{}_a$, $R^6{}_a$, R^7, A und B jeweils wie oben definiert sind und Ea eine aromatische, 6-gliedrige zyklische Gruppe (die 1 oder 2 Stickstoffatome im Ring enthalten kann) bedeutet, substituiert mit 1 bis 3 Substituenten Ga, die gleich oder verschieden voneinander sein können, worin Ga ein Halogenatom, C_{1-6}-Alkylgruppe, C_{1-6}-Alkoxygruppe, Hydroxylgruppe, Carboxylgruppe, die verestert oder amidiert sein kann, C_{1-6}-Alkylthiogruppe oder Phenoxygruppe ist, mit dem Vorbehalt, daß zumindest ein Ga an dem Ring eine Hydroxylgruppe ist, mit einer Verbindung der allgemeinen Formel (V)

X-Y (V)

worin X eine Gruppe ist, die mit dem Sauerstoffatom der Hydroxylgruppe binden kann, und Y eine entfernbare Gruppe bedeutet, oder mit einer anorganischen Säure oder organischen Säureanhydrid, die bzw. das mit der Hydroxylgruppe reaktiv ist, reagiert wird, wobei die Schutzgruppe, falls gewünscht, entfernt wird,

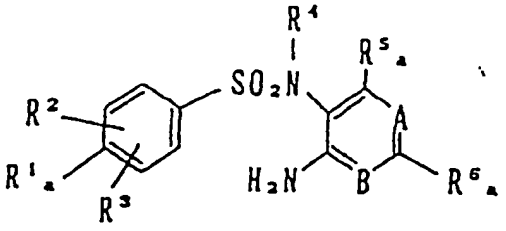
(c) ein Verfahren, worin eine Verbindung der allgemeinen Formel (VI)



(VI)

worin $R^1{}_a$, R^2, R^3, $R^5{}_a$, $R^6{}_a$, R^7, A, B und E jeweils wie oben definiert sind, mit einem Alkylierungsmittel reagiert wird, und wenn die resultierende Verbindung eine Schutzgruppe aufweist, diese Schutzgruppe, falls gewünscht, entfernt wird, und

(d) ein Verfahren, worin eine Verbindung der allgemeinen Formel (VII):



(VII)

worin $R^1{}_a$, R^2, R^3, R^4 , $R^5{}_a$, $R^6{}_a$, A und B jeweils wie oben definiert sind, mit einer Verbindung der allgemeinen

Formel (VIII):

$$R_{11}\text{-}Z \qquad \text{(VIII)}$$

worin R^{11} wie oben definiert ist und Z eine Carboxylgruppe bedeutet, oder mit dessen reaktivem Derivat reagiert wird oder wenn R^{11} eine C_{1-6}-Alkylaminogruppe ist, sie mit einem C_{1-6}-Alkylisocyanat reagiert wird.

9. Antineoplastisches Mittel, umfassend ein Sulfonamidderivat oder dessen pharmakologisch akzeptables Salz nach einem der Ansprüche 1 bis 7 als aktiven Bestandteil.

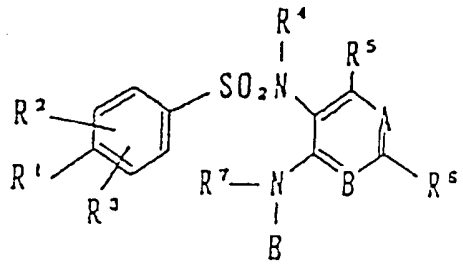
10. Sulfonamidderivate oder pharmakologisch akzeptable Salze davon nach einem der Ansprüche 1 bis 7, worin die Verbindung aus den folgenden Sulfonamidderivaten ausgewählt ist:

1) N- (2-Anilino-3-pyridyl)-p-toluolsulfonamid,
2) N-(2-Anilino-3-pyridyl)-4-ethylbenzolsulfonamid,
3) N-(2-Anilino-3-pyridyl)-4-methoxybenzolsulfonamid
4) 4-Methoxy-N-(2-((4-methoxyphenyl)amino)-3-pyridyl)benzolsulfonamid,
5) N-(2-((4-Hydroxyphenyl)amino) -3-pyridyl)-4-methoxybenzolsulfonamid,
6) 4-Methoxy-N-(2-((4-pyridyl)amino)-3-pyridyl)-benzolsulfonamid
7) 4- ((3- (4-Methoxybenzolsulfonamido)-2-pyridyl)-aminolphenyldihydrogenphosphat,
8) N- (2-Anilinophenyl)-4-methoxybenzolsulfonamid
9) N- (2- (4-Methoxybenzolsulfonamido)phenyl)-2-methylnicotinamid, und
10) N-(2-(4-Methoxybenzolsulfonamido)pehnyl)-3-methylisonicotinamid.

11. Pharmakologische Zusammensetzung, umfassend eine pharmakologisch effektive Menge des Derivates wie in einem der Ansprüche 1 bis 7 definiert und einen pharmakologisch akzeptablen Träger.

Revendications

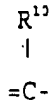
1. Dérivés de sulfonamide de formule génerale (I) ou sels pharmacologiquement acceptables de ceux-ci :



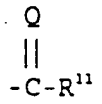
(I)

dans laquelle :

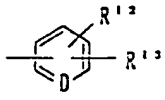
R^1 représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_{1-6}, un groupe alcoxy en C_{1-6}, un groupe hydroxy, un groupe nitro, un groupe phénoxy, un groupe cyano, un groupe acétyle ou un groupe amino qui peut être protégé,
R^2 et R^3 peuvent être identiques ou différents l'un de l'autre et représentent chacun un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_{1-6}, ou un groupe alcoxy en C_{1-6},
R^4 et R^7 peuvent être identiques ou différents l'un de l'autre et représentent chacun un atome d'hydrogène ou un groupe alkyle en C_{1-6},
R^5 et R^6 peuvent être identiques ou différents l'un de l'autre et représentent chacun un atome d'hydrogène, un atome d'halogène, un groupe alcoxy en C_{1-6} ou un groupe amino qui peut être substitué,
A représente un groupe de formule : =N- ou =CH-,
B représente un groupe de formule : =N- ou



dans laquelle R^{10} représente un atome d'hydrogène ou un groupe alkyle en C_{1-6},
E représente un groupe de formule :

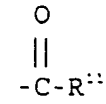


dans laquelle Q représente un atome d'oxygène ou un atome de soufre et R^{11} représente un atome d'hydrogène, un groupe alkyle en C_{1-6}, un groupe amino qui peut être substitué par un groupe alkyle en C_{1-6}, un groupe alcoxy en C_{1-6}, un groupe 2-thiényle, un groupe 2-furyle ou un groupe de formule :

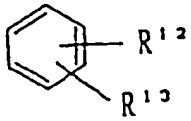


(D étant un groupe de formule : =N- ou =CH- et R^{12} et R^{13} étant identiques ou différents l'un de l'autre et représentant chacun un atome d'hydrogène, un atome d'halogène, un groupe nitro, un groupe hydroxy qui peut être protégé ou un groupe alkyle en C_{1-6}) ; ou un groupe cyclique aromatique à 6 chaînons qui peut être substitué par 1 à 3 substituants G qui peuvent être identiques ou différents les uns des autres, et lequel groupe cyclique peut comporter 1 ou 2 atomes d'azote dans son cycle (G représentant un atome d'halogène, un groupe alkyle en C_{1-6}, un groupe alcoxy en C_{1-6}, un groupe hydroxy qui peut être protégé, un groupe carboxy qui peut être estérifié ou amidifié, un groupe (alkyl en C_{1-6})thio ou un groupe phénoxy, à condition que les combinaisons suivantes soient exclues :

(1) une combinaison de R^1 qui est un atome d'hydrogène, un groupe alkyle en C_{1-6}, un groupe nitro ou un groupe amino qui peut être protégé, R^2 et R^3 qui représentent chacun un atome d'hydrogène, A et B qui représentent chacun =CH-et E qui représente un groupe phényle qui peut être substitué par 1 à 3 substituants G qui peuvent être identiques ou différents les uns des autres, et
(2) une combinaison de R^1, R^2 et R^3 qui peuvent être identiques ou différents les uns des autres et qui représentent chacun un atome d'hydrogène, un groupe alkyle en C_{1-6},un groupe nitro, un atome d'halogène ou un groupe acétylamino, A et B qui représentent chacun =CH-, et E qui représente un groupe de formule :



dans laquelle R^{11} représente un groupe alkyle en C_{1-6}, un groupe amino qui peut être substitué par un groupe alkyle en C_{1-6} ou un groupe de formule :



(R^{12} et R^{13} étant chacun tels que définis ci-dessus).

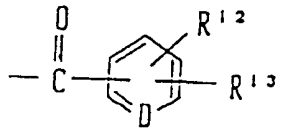
2. Dérivés de sulfonamide ou sels pharmacologiquement acceptables de ceux-ci selon la revendication 1, où R^1 représente un groupe alcoxy en C_{1-6}.

3. Dérivés de sulfonamide ou sels pharmacologiquement acceptables de ceux-ci selon la revendication 1, où A représente un groupe de formule : =CH- et B représente un groupe de formule : =N-.

4. Dérivés de sulfonamide ou sels pharmacologiquement acceptables de ceux-ci selon l'une quelconque des revendications 1 à 3, où E représente un groupe phényle, un groupe pyridyle ou un groupe pyrimidyle qui peut être substitué par 1 à 3 substituants G identiques ou différents (G étant tel que défini dans la revendication 1).

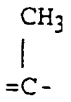
5. Dérivés de sulfonamide ou sels pharmacologiquement acceptables de ceux-ci selon l'une quelconque des revendications 1 à 3, où E représente un groupe phényle substitué par un groupe hydroxy qui peut être protégé.

6. Dérivés de sulfonamide ou sels pharmacologiquement acceptables de ceux-ci selon l'une quelconque des revendications 1 à 3, où A et B représentent chacun un groupe de formule : =CH-,
et E représente un groupe de formule :

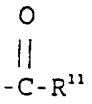


dans laquelle D, R^{12} et R^{13} sont chacun tels que définis ci-dessus.

7. Dérivés de sulfonamide ou sels pharmacologiquement acceptables de ceux-ci selon la revendication 1 ou 2, où A représente un groupe de formule : =CH-, B représente un groupe de formule :



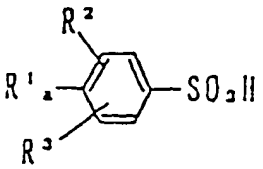
et E représente un groupe de formule :



dans laquelle R^{11} est tel que défini dans la revendication 1.

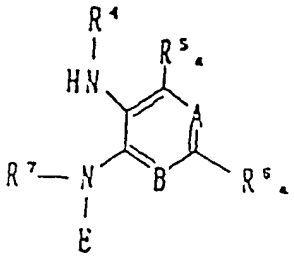
8. Procédé de production de dérivés de sulfonamide ou de sels pharmacologiquement acceptables de ceux-ci, selon l'une quelconque des revendications 1 à 7, par un quelconque des procédés (a) à (d) suivants :

(a) un procédé dans lequel on fait réagir un acide sulfonique de formule générale (II) ou son dérivé réactif :



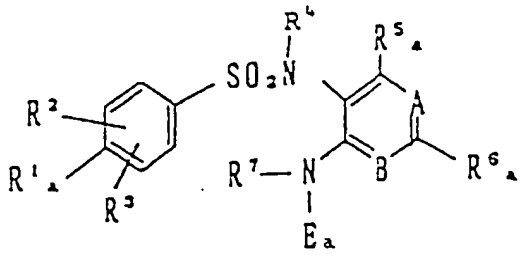
(II)

dans laquelle $R^1{}_a$ représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle en C_{1-6}, un groupe alcoxy en C_{1-6},un groupe hydroxy protégé, un groupe nitro, un groupe phénoxy, un groupe cyano, un groupe acétyle ou un groupe amino protégé, et R^2 et R^3 sont tels que définis dans la revendication 1,
avec un composé de formule générale (III) :



(III)

dans laquelle R^4, R^7, A, B et E sont tels que définis dans la revendication 1, et $R^5{}_a$ et $R^6{}_a$ peuvent être identiques ou différents l'un de l'autre et représentent chacun un atome d'hydrogène, un atome d'halogène, un groupe alcoxy en C_{1-6}, ou un groupe amino protégé ou substitué,
et quand le composé résultant a un groupe protecteur, on enlève, si on le souhaite, ledit groupe protecteur,
(b) un procédé dans lequel on fait réagir un composé de formule générale (IV)

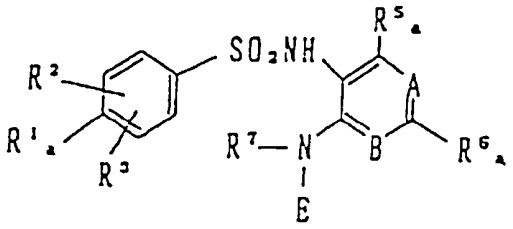


(IV)

dans laquelle $R^1{}_a$, R^2, R^3, R^4, $R^5{}_a$, $R^6{}_a$, R^7, A et B sont chacun tels que définis ci-dessus, et E_a représente un groupe cyclique aromatique à 6 chaînons (qui peut contenir 1 ou 2 atomes d'azote dans son cycle) substitué par 1 à 3 substituants G_a qui peuvent être identiques ou différents les uns des autres, G_a étant un atome d'halogène, un groupe alkyle en C_{1-6}, un groupe alcoxy en C_{1-6}, un groupe hydroxy, un groupe carboxy qui peut être estérifié ou amidifié, un groupe (alkyl en C_{1-6})thio ou un groupe phénoxy à condition qu'au moins un G_a sur le cycle soit un groupe hydroxy,
avec un composé de formule générale (V) :

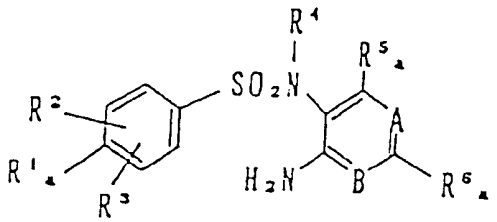
X-Y (V)

dans laquelle X représente un groupe capable de se lier avec l'atome d'oxygène du groupe hydroxy et Y représente un groupe pouvant être enlevé,
ou avec un acide inorganique ou anhydride d'acide organique réactif avec le groupe hydroxy et lorsque le composé résultant a un groupe protecteur, on enlève, si on le souhaite, ledit groupe protecteur,
(c) un procédé dans lequel on fait réagir un composé de formule générale (VI):



(VI)

dans laquelle $R^1{}_a$, R^2, R^3, $R^5{}_a$, $R^6{}_a$, R^7, A, B et E sont chacun tels que définis ci-dessus,
avec un agent d'alkylation et lorsque le composé résultant a un groupe protecteur, on enlève, si on le souhaite, ledit groupe protecteur,
et
(d) un procédé dans lequel on fait réagir un composé de formule générale (VII) :



(VII)

dans laquelle $R^1{}_a$, R^2, R^3, R^4, $R^5{}_a$, $R^6{}_a$, A et B sont chacun tels que définis ci-dessus,
avec un composé de formule générale (VIII) :

$$R^{11}\text{-}Z \qquad \text{(VIII)}$$

dans laquelle R^{11} est tel que défini ci-dessus, et Z représente un groupe carboxy ou son dérivé réactif,

ou lorsque R^{11} représente un groupe (alkyl en $C_{1\text{-}6}$)-amino, on le fait réagir avec un isocyanate d'(alkyle en $C_{1\text{-}6}$).

9. Agent anti-néoplasique comprend un dérivé de sulfonamide ou son sel pharmacologiquement acceptable selon l'une quelconque des revendications 1 à 7 comme constituant actif.

10. Dérivés de sulfonamide ou sels pharmacologiquement acceptables de ceux-ci, selon l'une quelconque des revendications 1 à 7, dans lesquels le composé est choisi parmi les dérivés de sulfonamide suivants :

1) le N-(2-anilino-3-pyridyl)-p-toluènesulfonamide,
2) le N-(2-anilino-3-pyridyl)-4-éthylbenzènesulfonamide,
3) le N-(2-anilino-3-pyridyl)-4-méthoxybenzènesulfonamide,
4) le 4-méthoxy-N-[2-[(4-méthoxyphényl)amino]-3-pyridyl]benzènesulfonamide,
5) le N-[2-[(4-hydroxyphényl)amino-3-pyridyl]-4-méthoxybenzènesulfonamide,
6) le 4-méthoxy-N-[2- [(4-pyridyl)amino]-3-pyridyl] benzènesulfonamide,
7) Le dihydrogéno phosphate de 4-[[3-(4-méthoxybenzènesulfonamido)-2-pyridyl] aminolphényle
8) le N-(2-anilinophényl)-4-méthoxybenzènesulfonamide,
9) le N-[2-(4-méthoxybenzènesulfonamido)phényl]-2-méthylnicotinamide,

et

10) le N- [2-(4-méthoxybenzénesulfonamido)phényl] -3-méthylisonicotinamide.

11. Composition pharmacologique qui comprend une quantité pharmacologiquement efficace du dérivé tel que défini dans l'une quelconque des revendications 1 à 7, et un véhicule pharmacologiquement acceptable.